De: Diego Ibáñez
A: normacov
Asunto: Antecedentes Norma COVs Diputado Diego Ibáñez.
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Junto con saludar, remito antecedentes para el proceso de elaboración de Norma de Calidad para compuestos orgánicos volátiles. Los antecedentes aportados consisten en el informe final y presentación del Colegio Médico en el marco de la Comisión Especial Investigadora de la Cámara de Diputados sobre las causas de la alta contaminación ambiental, especialmente en Concón, Quintero y Puchuncaví, y de las responsabilidades en la ejecución del Plan de Descontaminación, la cual presidí.

Adjunto además dos guías de calidad del aire de la Organización Mundial de la Salud y una de Reino Unido, las cuales contiene información sobre daños a la salud y concentraciones de COVs. Si bien parte de estas son específicamente para contaminación intradomiciliaria, las metodologías e información científica es de utilidad para definir niveles seguros en la normativa nacional.

Solicito acusar recibo de la información.

Sin otro particular se despide.

Diego Ibáñez Cotroneo
Diputado de la República
[redacted]

World Health Organization
Regional Office for Europe
Copenhagen

Air Quality Guidelines

for Europe

Second Edition

WHO Regional Publications, European Series, No. 91

Air quality guidelines for Europe, 2nd edition, 2000

CORRIGENDUM

On page 98, under Health risk evaluation, the second paragraph should read as follows.

In Germany a TDI for PCB of 1–3 μg/kg BW has been suggested. It was also recommended that, for precautionary reasons, the proportional daily intake via indoor air should not exceed 10% of the TDI for long periods. On this basis an action level for source removal of 3000 ng/m^3 has been derived. For concentrations between 3000 ng/m^3 and 10 000 ng/m^3 (that is, between 3 μg/m^3 and 10 μg/m^3) a concrete health risk is not assumed. However, mitigation measures should be undertaken as soon as possible to reduce the level to 300 ng/m^3, below which concentrations are thought to be of no concern. Source removal should also be undertaken if levels are found to be between 300 and 3000 ng/m^3 *(8)*.

The World Health Organization was established in 1948 as a specialized agency of the United Nations serving as the directing and coordinating authority for international health matters and public health. One of WHO's constitutional functions is to provide objective and reliable information and advice in the field of human health, a responsibility that it fulfils in part through its publications programmes. Through its publications, the Organization seeks to support national health strategies and address the most pressing public health concerns.

The WHO Regional Office for Europe is one of six regional offices throughout the world, each with its own programme geared to the particular health problems of the countries it serves. The European Region embraces some 870 million people living in an area stretching from Greenland in the north and the Mediterranean in the south to the Pacific shores of the Russian Federation. The European programme of WHO therefore concentrates both on the problems associated with industrial and post-industrial society and on those faced by the emerging democracies of central and eastern Europe and the former USSR.

To ensure the widest possible availability of authoritative information and guidance on health matters, WHO secures broad international distribution of its publications and encourages their translation and adaptation. By helping to promote and protect health and prevent and control disease, WHO's books contribute to achieving the Organization's principal objective – the attainment by all people of the highest possible level of health.

Air Quality Guidelines

for Europe

Second Edition

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WHO Regional Publications, European Series, No. 91

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Contents

Foreword

Clean air is considered to be a basic requirement for human health and wellbeing. In spite of the introduction of cleaner technologies in industry, energy production and transport, air pollution remains a major health risk. Recent epidemiological studies have provided evidence that in Europe hundreds of thousands of premature deaths are attributed to air pollution. The World Health Organization has been concerned with air pollution and its impact on human health for more than 40 years. In 1987 these activities culminated in the publication of the first edition of Air quality guidelines for Europe. *It was the aim of the guidelines to provide a basis for protecting public health from adverse effects of air pollutants, to eliminate or reduce exposure to hazardous air pollutants, and to guide national and local authorities in their risk management decisions. The guidelines were received with great enthusiasm and found wide application in environmental decision-making in the European Region as well as in other parts of the world.*

Since the publication of the first edition, new scientific data in the field of air pollution toxicology and epidemiology have emerged and new developments in risk assessment methodology have taken place. It was therefore necessary to update and revise the existing guidelines. Starting in 1993, the Bilthoven Division of the WHO European Centre for Environment and Health undertook this process in close cooperation with WHO headquarters and the European Commission. More than 100 experts contributed to the preparation of the background documents or participated in the scientific discussions that led to the derivation of guideline values for a great number of air pollutants. WHO is most grateful for their contribution and expert advice. Financial support received from the European Commission, the Swedish Environmental Protection Agency and the Government of the Netherlands during the preparation of the second edition of the guidelines made this effort possible and is warmly acknowledged.

The guidelines are a contribution to HEALTH*21, the health for all policy framework for the WHO European Region. This states that, by the year 2015, people in the Region should live in a safer physical environment, with exposure to contaminants hazardous to health at levels not exceeding internationally agreed standards. WHO is therefore pleased to see that the revised air quality*

guidelines are being used as a starting point for the derivation of legally binding limit values in the framework of the EU Air Quality Directive. Also, the global guidelines for air quality, recently issued by WHO headquarters, are based on the revised guidelines for Europe.

Thus, the work and efforts of everybody who contributed to the revision of the guidelines has already had an important impact. It is expected that the publication of this second edition will provide the Member States with a sound basis for improving human health by ensuring adequate air quality for all. I should like to warmly thank all the WHO staff who made this important endeavour possible.

Marc A. Danzon
WHO Regional Director for Europe

Preface

The first edition of the WHO *Air quality guidelines for Europe* was published in 1987. Since then new data have emerged and new developments in risk assessment methodology have taken place, necessitating the updating and revision of the existing guidelines. The Bilthoven Division of the WHO European Centre for Environment and Health has undertaken this process in close cooperation with the International Programme on Chemical Safety (IPCS) and the European Commission.

At the start of the process, the methods to be used in the risk assessment process, the use of the threshold concept, the application of uncertainty factors, and the quantitative risk assessment of carcinogens were discussed, and the approach to be used was agreed on. In setting priorities for the compounds to be reviewed, a number of criteria were established: (*a*) the compound (or mixture) posed a widespread problem in terms of exposure sources; (*b*) the potential for personal exposure was large; (*c*) new data on health or environmental impact had emerged; (*d*) monitoring had become feasible since the previous evaluation; and (*e*) a positive trend in ambient air concentrations was evident. Application of these criteria has resulted in the selection of the air pollutants addressed in the review process.

It is the aim of the guidelines to provide a basis for protecting public health from adverse effects of air pollutants and to eliminate or reduce exposure to those pollutants that are known or likely to be hazardous to human health or wellbeing. The guidelines are intended to provide background information and guidance to (inter)national and local authorities in making risk assessment and risk management decisions. In establishing pollutant levels below which exposure – for life or for a given period of time – does not constitute a significant public health risk, the guidelines provide a basis for setting standards or limit values for air pollutants.

Although the guidelines are considered to be protective to human health they are by no means a "green light" for pollution, and it should be stressed that attempts should be made to keep air pollution levels as low as practically achievable. In addition, it should be noted that in general the guidelines do not differentiate between indoor and outdoor air exposure because,

although the site of exposure determines the composition of the air and the concentration of the various pollutants, it does not directly affect the exposure–response relationship.

In general, the guidelines address single pollutants, whereas in real life exposure to mixtures of chemicals occurs, with additive, synergistic or antagonistic effects. In dealing with practical situations or standard-setting procedures, therefore, consideration should be given to the interrelationships between the various air pollutants. It should be emphasized, however, that the guidelines are health-based or based on environmental effects, and are not standards *per se*. In setting legally binding standards, considerations such as prevailing exposure levels, technical feasibility, source control measures, abatement strategies, and social, economic and cultural conditions should be taken into account.

It is a policy issue to decide which specific groups at risk should be protected by the standards and what degree of risk is considered to be acceptable. These decisions are influenced by differences in risk perception among the general population and the various stakeholders in the process, but also by differences in social situations in different countries, and by the way the risks associated with air pollution are compared with risks from other environmental exposures or human activities. National standards may therefore differ from country to country and may be above or below the respective WHO guideline value.

This publication includes an introduction on the nature of the guidelines and the methodology used to establish guideline values for a number of air pollutants. In addition, it describes the various aspects that need to be considered by national or local authorities when guidelines are transformed into legally binding standards. For the pollutants addressed, the sections on "Health risk evaluation" and "Guidelines" describe the most relevant considerations that have led to the recommended guideline values. For detailed information on exposure and on the potential health effects of the reviewed pollutants, the reader is referred to the Regional Office's web site, where the background documents on the individual air pollutants can be accessed.

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PART I

GENERAL

CHAPTER 1

Introduction

Human beings need a regular supply of food and water and an essentially continuous supply of air. The requirements for air and water are relatively constant (10–20 m^3 and 1–2 litres per day, respectively). That all people should have free access to air and water of acceptable quality is a fundamental human right. Recognizing the need of humans for clean air, in 1987 the WHO Regional Office for Europe published *Air quality guidelines for Europe (1)*, containing health risk assessments of 28 chemical air contaminants.

These guidelines can be seen as a contribution to target 10 of HEALTH21, the health for all policy framework for the WHO European Region as formulated in 1999 *(2)*. This target states that by the year 2015, people in the Region should live in a safer physical environment, with exposure to contaminants hazardous to health at levels not exceeding internationally agreed standards. The achievement of this target will require the introduction of effective legislative, administrative and technical measures for the surveillance and control of both outdoor and indoor air pollution, in order to comply with criteria to safeguard human health. Unfortunately, this ambitious objective is not likely to be met in the next few years in many areas of Europe. Improvement in epidemiological research over the 1990s and greater sensitivity of the present studies have revealed that people's health may be affected by exposures to much lower levels of some common air pollutants than believed even a few years ago. While the no-risk situation is not likely to be achieved, a minimization of the risk should be the objective of air quality management, and this is probably a major conceptual development of the last few years.

Various chemicals are emitted into the air from both natural and man-made (anthropogenic) sources. The quantities may range from hundreds to millions of tonnes annually. Natural air pollution stems from various biotic and abiotic sources such as plants, radiological decomposition, forest fires, volcanoes and other geothermal sources, and emissions from land and water. These result in a natural background concentration that varies according to local sources or specific weather conditions. Anthropogenic air pollution has existed at least since people learned to use fire, but it has

increased rapidly since industrialization began. The increase in air pollution resulting from the expanding use of fossil energy sources and the growth in the manufacture and use of chemicals has been accompanied by mounting public awareness of and concern about its detrimental effects on health and the environment. Moreover, knowledge of the nature, quantity, physico-chemical behaviour and effects of air pollutants has greatly increased in recent years. Nevertheless, more needs to be known. Certain aspects of the health effects of air pollutants require further assessment; these include newer scientific areas such as developmental toxicity. The proposed guideline values will undoubtedly be changed as future studies lead to new information.

The impact of air pollution is broad. In humans, the pulmonary deposition and absorption of inhaled chemicals can have direct consequences for health. Nevertheless, public health can also be indirectly affected by deposition of air pollutants in environmental media and uptake by plants and animals, resulting in chemicals entering the food chain or being present in drinking-water and thereby constituting additional sources of human exposure. Furthermore, the direct effects of air pollutants on plants, animals and soil can influence the structure and function of ecosystems, including their self-regulation ability, thereby affecting the quality of life.

In recent decades, major efforts have been made to reduce air pollution in the European Region. The emission of the main air pollutants has declined significantly. The most pronounced effect is observed for sulfur dioxide: its total emission was reduced by about 50% in the period 1980–1995. Reduction of emission of nitrogen oxides was smaller and was observed only after 1990: total emission declined by about 15% in the period from 1990 to 1995 *(3)*. The reduction of sulfur dioxide emission is reflected by declining concentrations in ambient air in urban areas. Trends in concentrations of other pollutants in urban air, such as nitrogen dioxide or particulate matter, are less clear and it is envisaged that these pollutants still constitute a risk to human health *(4)*.

Many countries of the European Region encounter similar air pollution problems, partly because pollution sources are similar, and in any case air pollution does not respect national frontiers. The subject of the transboundary long-range transport of air pollution has received increasing attention in Europe over the last decade. International efforts to combat emissions are undertaken, for instance within the framework of the Convention on Long-range Transboundary Air Pollution established by the United Nations Economic Commission for Europe *(5, 6)*.

The task of reducing levels of exposure to air pollutants is a complex one. It begins with an analysis to determine which chemicals are present in the air, at what levels, and whether likely levels of exposure are hazardous to human health and the environment. It must then be decided whether an unacceptable risk is present. When a problem is identified, mitigation strategies should be developed and implemented so as to prevent excessive risk to public health in the most efficient and cost-effective way.

Analyses of air pollution problems are exceedingly complicated. Some are national in scope (such as the definition of actual levels of exposure of the population, the determination of acceptable risk, and the identification of the most efficient control strategies), while others are of a more basic character and are applicable in all countries (such as analysis of the relationships between chemical exposure levels, and doses and their effects). The latter form the basis of these guidelines.

The most direct and important source of air pollution affecting the health of many people is tobacco smoke. Even those who do not smoke may inhale the smoke produced by others ("passive smoking"). Indoor pollution in general and occupational exposure in particular also contribute substantially to overall human exposure: indoor concentrations of nitrogen dioxide, carbon monoxide, respirable particles, formaldehyde and radon are often higher than outdoor concentrations *(7)*.

Outdoor air pollution can originate from a single point source, which may affect only a relatively small area. More often, outdoor air pollution is caused by a mixture of pollutants from a variety of diffuse sources, such as traffic and heating, and from point sources. Finally, in addition to those emitted by local sources, pollutants transported over medium and long distances contribute further to the overall level of air pollution.

The relative contribution of emission sources to human exposure to air pollution may vary according to regional and lifestyle factors. Although, as far as some pollutants are concerned, indoor air pollution will be of greater importance than outdoor pollution, this does not diminish the importance of outdoor pollution. In terms of the amounts of substances released, the latter is far more important and may have deleterious effects on animals, plants and materials as well as adverse effects on human health. Pollutants produced outdoors may penetrate into the indoor environment and may affect human health by exposure both indoors and outdoors.

NATURE OF THE GUIDELINES

The primary aim of these guidelines is to provide a basis for protecting public health from adverse effects of air pollution and for eliminating, or reducing to a minimum, those contaminants of air that are known or likely to be hazardous to human health and wellbeing. In the present context, guidelines are not restricted to a numerical value below which exposure for a given period of time does not constitute a significant health risk; they also include any kind of recommendation or guidance in the relevant field.

The guidelines are intended to provide background information and guidance to governments in making risk management decisions, particularly in setting standards, but their use is not restricted to this. They also provide information for all who deal with air pollution. The guidelines may be used in planning processes and various kinds of management decisions at community or regional level.

When guideline values are indicated, this does not necessarily mean that they should be used as the starting point for producing general countrywide standards, monitored by a comprehensive network of control stations. In the case of some pollutants, guideline values may be of use mainly for carrying out local control measures around point sources. To aid in this process, information on major sources of pollutants has been provided.

It should be emphasized that when numerical air quality guideline values are given, these values are not standards in themselves. Before transforming them into legally binding standards, the guideline values must be considered in the context of prevailing exposure levels, technical feasibility, source control measures, abatement strategies, and social, economic and cultural conditions (see Chapter 4). In certain circumstances there may be valid reasons to pursue policies that will result in pollutant concentrations above or below the guideline values.

Although these guidelines are considered to protect human health, they are by no means a "green light" for pollution. It should be stressed that attempts should be made to keep air pollution levels as low as practically achievable.

Ambient air pollutants can cause a range of significant effects that require attention: irritation, odour annoyance, and acute and long-term toxic effects. Numerical air quality guidelines either indicate levels combined with exposure times at which no adverse effect is expected in terms of noncarcinogenic endpoints, or they provide an estimate of lifetime cancer risk arising from those substances that are proven human carcinogens or

carcinogens with at least limited evidence of human carcinogenicity. It should be noted that the risk estimates for carcinogens do not indicate a safe level, but they are presented so that the carcinogenic potencies of different carcinogens can be compared and an assessment of overall risk made.

It is believed that inhalation of an air pollutant in concentrations and for exposure times below a guideline value will not have adverse effects on health and, in the case of odorous compounds, will not create a nuisance of indirect health significance. This is in line with the definition of health: a state of complete physical, mental and social wellbeing and not merely the absence of disease or infirmity *(8)*. Nevertheless, compliance with recommendations regarding guideline values does not guarantee the absolute exclusion of effects at levels below such values. For example, highly sensitive groups such as those impaired by concurrent disease or other physiological limitations may be affected at or near concentrations referred to in the guideline values. Health effects at or below guideline values may also result from combined exposure to various chemicals or from exposure to the same chemical by multiple routes.

It is important to note that guidelines have been established for single chemicals. Mixtures of chemicals can have additive, synergistic or antagonistic effects. In general, our knowledge of these interactions is rudimentary. One exception can be found in a WHO publication on summer and winter smog *(9)*, which deals with commonly recurring mixtures of air pollutants.

In preparing this second edition of the guidelines, emphasis has been placed on providing data on the exposure–response relationships of the pollutants considered. It is expected that this will provide a basis for estimating the risk to health posed by monitored concentrations of these pollutants.

Although health effects were the major consideration in establishing the guidelines, evidence of the effects of pollutants on terrestrial vegetation was also considered and guideline values were recommended for a few substances (see Part III). These ecological guidelines have been established because, in the long term, only a healthy total environment can guarantee human health and wellbeing. Ecological effects on life-forms other than humans and plants have not been discussed since they are outside the scope of this book.

The guidelines do not differentiate between indoor and outdoor exposure (with the exception of exposure to mercury) because, although the sites of

exposure influence the type and concentration of air pollutants, they do not directly affect the basic exposure–effect relationships. Occupational exposure has been considered in the evaluation process, but it was not a main focus of attention as these guidelines relate to the general population. However, it should be noted that occupational exposure may add to the effects of environmental exposure. The guidelines do not apply to very high short-term concentrations that may result from accidents or natural disasters.

The health effects of tobacco smoking have not been assessed here, the carcinogenic effects of smoking having already been evaluated by IARC in 1986 *(10)*. Neither have the effects of air pollutants on climate been considered, since too many uncertainties remain to allow a satisfactory evaluation of possible adverse health and environmental effects. Possible changes of climate, however, should be investigated very seriously by the appropriate bodies because their overall consequences, for example the "greenhouse effect", may go beyond direct adverse effects on human health or ecosystems.

PROCEDURES USED IN THE UPDATING AND REVISION PROCESS

The first step in the process of updating and revising the guidelines was the selection of pollutants. Air pollutants of special environmental and health significance to countries of the European Region were identified and selected by a WHO planning group in 1993 *(11)* on the basis of the following criteria:

(*a*) whether substances or mixtures posed a widespread problem in terms of sources;
(*b*) the ubiquity and abundance of the pollutants where the potential for exposure was large, taking account of both outdoor and indoor exposure;
(*c*) whether significant new information on health effects had become available since the publication of the first edition of the guidelines;
(*d*) the feasibility of monitoring;
(*e*) whether significant non-health (e.g. ecotoxic) effects could occur; and
(*f*) whether a positive trend in ambient levels was evident.

During the deliberations of the planning group, compounds that had not been dealt with in the first edition of the guidelines were also

considered, including butadiene, fluoride, compounds associated with global warming and with alterations in global air pollution (and possibly with secondary health effects), and compounds associated with the development of alternative fuels and new fuel additives. Other factors affecting selection included the timetable of the project, and the fact that only those substances for which sufficient documentation was available could be considered.

The existence of relevant WHO Environmental Health Criteria documents was of great value in this respect. On the basis of these considerations, the following 35 pollutants were selected to be included in this second edition of the guidelines:

Organic air pollutants
Acrylonitrile[1]
Benzene
Butadiene
Carbon disulfide[1]
Carbon monoxide
1,2-Dichloroethane[1]
Dichloromethane
Formaldehyde
Polycyclic aromatic hydrocarbons (PAHs)
Polychlorinated biphenyls (PCBs)
Polychlorinated dibenzodioxins and dibenzofurans (PCDDs/PCDFs)
Styrene
Tetrachloroethylene
Toluene
Trichloroethylene
Vinyl chloride[1]

Indoor air pollutants
Environmental tobacco smoke
Man-made vitreous fibres
Radon

Inorganic air pollutants
Arsenic
Asbestos[1]
Cadmium
Chromium
Fluoride
Hydrogen sulfide[1]
Lead
Manganese
Mercury
Nickel
Platinum
Vanadium[1]

Classical air pollutants
Nitrogen dioxide
Ozone and other photochemical oxidants
Particulate matter
Sulfur dioxide

[1] 1987 evaluation retained, not re-evaluated.

In addition to the 35 pollutants listed above, this second edition expands on the ecological effects presented in the first edition in an enlarged section examining the ecotoxic effects of sulfur dioxide (including sulfur and total acid deposition), nitrogen dioxide (and other nitrogen compounds, including ammonia) and ozone.

To carry out the evaluation process, the planning group established a number of working groups on:

- methodology and format
- ecotoxic effects
- classical air pollutants
- inorganic air pollutants
- certain indoor air pollutants
- polychlorinated biphenyls, dioxins and furans
- volatile organic pollutants.

The dates of the meetings of these working groups and the membership are listed in Annex I.

Before the meeting of each working group, scientific background documents providing in-depth reviews of each pollutant were prepared as a basis for discussion. Guidelines were established on the basis of these discussions. After each meeting, a text on each pollutant or pollutant group was drafted on the basis of the amended background documents, incorporating the working group's conclusions and recommendations. The draft report of the working group was then circulated to all participants for their comments and corrections. A final consultation group was then convened to critically review the documents for clarity of presentation, adequacy of description of the rationale supporting each guideline and consistency in the application of criteria, and with a view to possibly considering newly emerged information. The process concluded with a review of the recommendations and conclusions of all the working groups.

It was appreciated, during preparation of this second edition, that the expanded range of pollutants being considered and the considerably expanded database available for some pollutants would lead to a significant lengthening of the text. It was therefore decided to publish in this volume summaries of the data on which the guidelines are based. The full background evaluation will become progressively available on the Regional Office's web site.

As in the first edition, detailed referencing of the relevant literature has been provided with indications of the periods covered by the reviews of individual pollutants. Every effort has been made to ensure that the material provided is as up-to-date as possible, although the extended period of preparation of this second edition has inevitably meant that some sections refer to more recently published material than others.

During the preparation of the second edition, the Directorate-General for Environment, Nuclear Safety and Civil Protection (DGXI) of the European Commission developed a Framework Directive and a number of daughter directives dealing with individual pollutants. It was agreed with the Commission that the final drafts of the revised WHO guideline documents would provide a starting point for discussions by the Commission's working groups aiming at setting legally binding limit values for air quality in the European Union.

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CHAPTER 2

Criteria used in establishing guideline values

Relevant information on the pollutants was carefully considered during the process of establishing guideline values. Ideally, guideline values should represent concentrations of chemical compounds in air that would not pose any hazard to the human population. Realistic assessment of human health hazards, however, necessitates a distinction between absolute safety and acceptable risk. To produce a guideline with a high probability of offering absolute safety, one would need a detailed knowledge of dose–response relationships in individuals in relation to all sources of exposure, the types of toxic effect elicited by specific pollutants or their mixtures, the existence or nonexistence of "thresholds" for specified toxic effects, the significance of interactions, and the variation in sensitivity and exposure levels within the human population. Such comprehensive and conclusive data on environmental contaminants are generally unavailable. Very often the relevant data are scarce and the quantitative relationships uncertain. Scientific judgement and consensus therefore play an important role in establishing guidance that can be used to indicate acceptable levels of population exposure. Value judgements are needed and the use of subjective terms such as "adverse effects" and "sufficient evidence" is unavoidable.

Although it may be accepted that a certain risk can be tolerated, the risks to individuals within a population may not be equally distributed: there may be subpopulations that are at considerably increased risk. Therefore, groups at special risk in the general population must be taken specifically into account in the risk management process. Even if knowledge about groups with specific sensitivity is available, unknown factors may exist that change the risk in an unpredictable manner. During the preparation of this second edition of the guidelines, attention has been paid to defining specific sensitive subgroups in the population.

INFORMATION COMMON TO CARCINOGENS AND NONCARCINOGENS

Sources, levels and routes of exposure

Available data are provided on the current levels of human exposure to pollutants from all sources, including the air. Special attention is given to

atmospheric concentrations in urban and unpolluted rural areas and in the indoor environment. Where appropriate, concentrations in the workplace are also indicated for comparison with environmental levels. To provide information on the contribution from air in relation to all other sources, data on uptake by inhalation, ingestion from water and food, and dermal contact are given where relevant. For most chemicals, however, data on total human exposure are incomplete.

Toxicokinetics

Available data on toxicokinetics (absorption, distribution, metabolism and excretion) of air pollutants in humans and experimental animals are provided for comparison between test species and humans and for interspecies and intraspecies extrapolation, especially to assess the magnitude of body burden from long-term, low-level exposures and to characterize better the mode of toxic action. Data concerning the distribution of a compound in the body are important in determining the molecular or tissue dose to target organs. It has been appreciated that high-to-low-dose and interspecies extrapolations are more easily carried out using equivalent tissue doses. Metabolites are mentioned, particularly if they are known or believed to exert a greater toxic potential than the parent compound. Additional data of interest in determining the fate of a compound in a living organism include the rate of excretion and the biological half-life. These toxicokinetic parameters should be compared between test species and humans for derivation of interspecies factors where this is possible.

Terminology

The following terms and definitions are taken largely from Environmental Health Criteria No. 170, 1994 *(1)*.

Adverse effect Change in morphology, physiology, growth, development or life span of an organism which results in impairment of functional capacity or impairment of capacity to compensate for additional stress or increase in susceptibility to the harmful effects of other environmental influences.

Benchmark dose (BMD) The lower confidence limit of the dose calculated to be associated with a given incidence (e.g. 5% or 10% incidence) of effect estimated from all toxicity data on that effect within that study *(2)*.

Critical effect(s) The adverse effect(s) judged to be most appropriate for the health risk evaluation.

Lowest-observed-adverse-effect level (**LOAEL**) Lowest concentration or amount of a substance, found by experiment or observation, which causes an adverse alteration of morphology, functional capacity, growth, development or life span of the target organism distinguishable from normal (control) organisms of the same species and strain under the same defined conditions of exposure.

No-observed-adverse-effect level (**NOAEL**) Greatest concentration or amount of a substance, found by experiment or observation, which causes no detectable adverse alteration of morphology, functional capacity, growth, development or life span of the target organism under defined conditions of exposure. Alterations of morphology, functional capacity, growth, development or life span of the target may be detected which are judged not to be adverse.

Toxicodynamics The process of interaction of chemical substances with target sites and the subsequent reactions leading to adverse effects.

Toxicokinetics The process of the uptake of potentially toxic substances by the body, the biotransformation they undergo, the distribution of the substances and their metabolites in the tissues, and the elimination of the substances and their metabolites from the body. Both the amounts and the concentrations of the substances and their metabolites are studied. The term has essentially the same meaning as pharmacokinetics, but the latter term should be restricted to the study of pharmaceutical substances.

Uncertainty factor (**UF**) A product of several single factors by which the NOAEL or LOAEL of the critical effect is divided to derive a tolerable intake. These factors account for adequacy of the pivotal study, interspecies extrapolation, inter-individual variability in humans, adequacy of the overall database, and nature of toxicity. The choice of UF should be based on the available scientific evidence.

CRITERIA FOR ENDPOINTS OTHER THAN CARCINOGENICITY

Criteria for selection of NOAEL/LOAEL

For those compounds reportedly without direct carcinogenic effects, determination of the highest concentration at which no adverse effects are observed, or the lowest concentration at which adverse effects are observed in humans, animals or plants is the first step in the derivation of the guideline value. This requires a thorough evaluation of available data on toxicity. The

decision as to whether the LOAEL or the NOAEL should be used as a starting point for deriving a guideline value is mainly a matter of availability of data. If a series of data fixes both the LOAEL and the NOAEL, then either might be used. The gap between the lowest-observed-effect level and the no-observed-effect level is among the factors included in judgements concerning the appropriate uncertainty factor. Nevertheless, one needs to consider that in studies in experimental animals, the value of the NOAEL (or LOAEL) is an observed value that is dependent on the protocol and design of the study from which it was derived. There are several factors that influence the magnitude of the value observed, such as the species, sex, age, strain and developmental status of the animals studied; the group size; the sensitivity of the methods applied; and the selection of dose levels. Dose levels are frequently widely spaced, so that the observed NOAEL can be in some cases considerably less than the true no-adverse-effect level, and the observed LOAEL considerably higher than the true lowest-adverse-effect level *(1)*.

A single, free-standing no-observed-effect level that is not defined in reference to a lowest-observed-effect level or a LOAEL is not helpful. It is important to understand that, to be useful in setting guidelines, the NOAEL must be the highest level of exposure at which no adverse effects are detected. It is difficult to be sure that this has been identified unless the level of exposure at which adverse effects begin to appear has also been defined. Opinions on this subject differ, but the working consensus was that the level of exposure of concern in terms of human health is more easily related to the LOAEL, and this level was therefore used whenever possible. In the case of irritant and sensory effects on humans, it is desirable where possible to determine the no-observed-effect level. These effects are discussed in more detail below.

On the basis of the evidence concerning adverse effects, judgements about the uncertainty factors needed to minimize health risks were made. Averaging times were included in the specification of the guidelines, as the duration of exposure is often critical in determining toxicity. Criteria applied to each of these key factors are described below.

Criteria for selection of adverse effect

Definition of a distinction between adverse and non-adverse effects poses considerable difficulties. Any observable biological change might be considered an adverse effect under certain circumstances. An adverse effect has been defined as "any effect resulting in functional impairment and/or pathological lesions that may affect the performance of the whole organism or

which contributes to a reduced ability to respond to an additional challenge" *(3)*. Even with such a definition, a significant degree of subjectivity and uncertainty remains. Ambient levels of major air pollutants frequently cause subtle effects that are typically detected only by sensitive methods. This makes it exceedingly difficult, if not impossible, to achieve a broad consensus as to which effects are adverse. To resolve this difficulty, it was agreed that the evidence should be ranked in three categories.

1. The first category comprises observations, even of potential health concern, that are single findings not verified by other groups. Because of the lack of verification by other investigators, such data could not readily be used as a basis for deriving a guideline value. They do, however, indicate the need for further research and may be considered in deriving an appropriate uncertainty factor based on the severity of the observed effects.

2. The second category is a lowest-observed-effect level (or no-observed-effect level) that is supported by other scientific information. When the results are in a direction that might result in pathological changes, there is a higher degree of health concern. Scientific judgement based on all available health information is used to determine how effects in this category can be used in determining the pollutant level that should be avoided so that excessive risk can be prevented.

3. The third category comprises levels of exposure at which there is clear evidence for substantial pathological changes; these findings have had a major influence on the derivation of the guidelines.

Benchmark approach

The benchmark dose (BMD) is the lower confidence limit of the dose that produces a given increase (e.g. 5% or 10%) in the level of an effect to which an uncertainty factor can be applied to develop a tolerable intake. It has a number of advantages over the NOAEL/LOAEL approach *(2)*. First, the BMD is derived on the basis of the entire dose–response curve for the critical, adverse effect rather than that from a single dose group as in the case of the NOAEL/LOAEL. Second, it can be calculated from data sets in which a NOAEL was not determined, eliminating the need for an additional uncertainty factor to be applied to the LOAEL. Third, definition of the BMD as a lower confidence limit accounts for the statistical power and quality of the data; that is, the confidence intervals around the dose–response curve for studies with small numbers of animals or of poor quality and thus lower statistical power would be wide, reflecting the greater

uncertainty of the database. On the other hand, better studies would result in narrow confidence limits, and thus in higher BMDs.

Although there is no consensus on the incidence of effect to be used as basis for the BMD, it is generally agreed that the BMD should be comparable with a level of effect typically associated with the NOAEL or LOAEL. Allen et al. *(4, 5)* have estimated that a BMD calculated from the lower confidence limit at 5% is, on average, comparable to the NOAEL, whereas choosing a BMD at 10% is more representative of a LOAEL *(6)*. Choosing a BMD that is comparable to the NOAEL has two advantages: (*a*) it is within the experimental dose-range, eliminating the need to interpolate the dose–response curve to low levels; and (*b*) it justifies the application of similar uncertainty factors as are currently applied to the NOAEL for interspecies and intraspecies variation. It should be noted, however, that the main disadvantage of the benchmark approach is that it is not applicable for discrete toxicity data, such as histopathological or teratogenicity data.

Criteria for selection of uncertainty factors

In previous evaluations by WHO, uncertainty factors (sometimes called safety factors) have been applied to derive guidelines from evidence that conforms to accepted criteria for adverse effects on health *(7–9)*. Traditionally, the uncertainty (safety) factor has been used to allow for uncertainties in extrapolation from animals to humans and from a small group of individuals to a large population, including possibly undetected effects on particularly sensitive members of the population. In addition, uncertainty factors also account for possible synergistic effects of multiple exposures, the seriousness of the observed effects and the adequacy of existing data *(1)*. It is important to understand that the application of such factors does not indicate that it is known that humans are more sensitive than animal species but, rather, that the sensitivity of humans relative to that of other species is usually unknown. It is possible that humans are less sensitive than animals to some chemicals.

In this second edition of the air quality guidelines, the terms "safety factor" and "protection factor" have been replaced by the term "uncertainty factor". It is felt that this better explains the derivation and implications of such factors. Of course, such a factor is designed to provide an adequate level of protection and an adequate margin of safety, because these factors are applied in the derivation of guidelines for the protection of human health. They are not applied in the derivation of ecological guidelines because these already include a kind of uncertainty factor with regard to the variety of species covered.

A wide range of uncertainty factors are used in this second edition, based on scientific judgements concerning the interplay of various effects. The decision process for developing uncertainty factors has been complex, involving the transformation of mainly non-quantitative information into a single number expressing the judgement of a group of scientists.

Some of the factors taken into account in deciding the margin of protection can be grouped under the heading of scientific uncertainty. Uncertainty occurs because of limitations in the extent or quality of the database. One can confidently set a lower margin of protection (that is, use a smaller uncertainty factor) when a large number of high-quality, mutually supportive scientific experiments in different laboratories using different approaches clearly demonstrate the dose–response, including a lowest-observed-effect level and a no-observed-effect level. In reality, difficulties inherent in studying air pollutants, and the failure to perform much-needed and very specific research, means that often a large uncertainty factor has to be applied.

Where an uncertainty factor was adopted in the derivation of air quality guidelines, the reasoning behind the choice of this factor is given in the scientific background information. As previously mentioned, exceeding a guideline value with an incorporated uncertainty factor does not necessarily mean that adverse effects will result. Nevertheless, the risk to public health will increase, particularly in situations where the most sensitive population group is exposed to several pollutants simultaneously.

Individuals and groups within a population show marked differences in sensitivity to given pollutants. Individuals with pre-existing lung disease, for instance, may be at higher risk from exposure to air pollutants than healthy people. Differences in response can be due to factors other than pre-existing health, including age, sex, level of exercise taken and other unknown factors. Thus, the population must be considered heterogeneous in respect of response to air pollutants. This perhaps wide distribution of sensitivity combined with a distribution of exposure makes the establishment of population-based thresholds of effect very difficult. This problem is taken up in the section on particulate matter (page 186). Existing information tends not to allow adequate assessment of the proportion of the population that is likely to show an enhanced response. Nevertheless, an estimate of even a few percent of the total population entails a large number of people at increased risk.

Deriving a guideline from studies of effects on laboratory animals in the absence of human studies generally requires the application of an increased

uncertainty factor, because humans may be more susceptible than laboratory animal species. Negative data from human studies will tend to reduce the magnitude of this uncertainty factor. Also of importance are the nature and reversibility of the reported effect. Deriving a guideline from data that show that a given level of exposure produces only slight alterations in physiological parameters requires a smaller uncertainty factor than when data showing a clearly adverse effect are used. Scientific judgement about uncertainty factors should also take into account the biochemical toxicology of pollutants, including the types of metabolite formed, the variability in metabolism or response in humans suggesting the existence of hypersusceptible groups, and the likelihood that the compound or its metabolites will accumulate in the body.

It is obvious, therefore, that diverse factors must be taken into account in proposing a margin of protection. The uncertainty factor cannot be assigned by a simple mathematical formula; it requires experience, wisdom and judgement.

Feasibility of adopting a standard approach

In preparing this second edition of the guidelines, the feasibility of developing a standard methodology for setting guidelines was discussed. It was agreed that Environmental Health Criteria No. 170 *(1)* was a valuable source of information. On the other hand, it was recognized that large variation in the data available for different compounds made the use of a standard approach impossible. Much of the difficulty concerns the adequacy of the database, and this has played a large part in controlling the methods of assessment adopted. This is illustrated in Table 1.

Table 1. Size and completeness of database in relation to assessment method

Examples	Completeness/ size of database	Uncertainties	Feasibility of expert judgement	Need for standardized approach
Nitrogen dioxide, ozone, lead	+++	+	+++	+
Manganese, nickel	++	++	++	++
Volatile organic compounds	+	+++	+	+++

It will be seen that when the database is strong (that is, when a good deal is known about the human toxicology of the compound) it is suggested that expert judgement can be used to set a guideline. In such circumstances the level of uncertainty is low. If, on the other hand, the database is weak, then a larger level of uncertainty will exist and there is much to be said for using a standardized approach, probably involving the application of a substantial uncertainty factor. The dangers of replacing expert judgement and the application of common sense with advanced, complex and sometimes not intuitively obvious statistical methods for deriving guidelines was discussed. It was agreed that a cautious approach should be adopted.

Criteria for selection of averaging times

The development of toxicity is a complex function of the interaction between concentration of a pollutant and duration of exposure. A chemical may cause acute, damaging effects after peak exposure for a short period and irreversible or incapacitating effects after prolonged exposure to lower concentrations. Our knowledge is usually insufficient to define accurately the relationship between effects on the one hand and concentration and time on the other. Expert judgement must be applied, therefore, based on the weight of the evidence available *(10)*.

Generally, when short-term exposures lead to adverse effects, short-term averaging times are recommended. The use of a long-term average under such conditions would be misleading, since the typical pattern of repeated peak exposures is lost during the averaging process and the risk manager would have difficulties in deciding on effective strategies. In other cases, knowledge of the exposure–response relationship may be sufficient to allow recommendation of a long averaging period. This is frequently the case for chemicals that accumulate in the body and thereby produce adverse effects. In such cases, the integral of concentration over a long period can have more impact than the pattern of peak exposure.

It should be noted that the specified averaging times are based on effects on health. Therefore, if the guidelines are used as a basis for regulation, the regulator needs to select the most appropriately and practically defined standards in relation to the guidelines, without necessarily adopting the guidelines directly. It was appreciated that monitoring techniques for some pollutants would not allow reporting of data in terms of the averaging times recommended in the guidelines. Under such circumstances, a compromise between the averaging time specified in the guidelines and that obtainable in practice has to be reached in setting an air quality standard.

A similar situation occurs for effects on vegetation. Plants are generally damaged by short-term exposures to high concentration as well as by long-term exposures to low concentration. Therefore, both short- and long-term guidelines to protect plants are proposed.

Criteria for consideration of sensory effects

Some of the substances selected for evaluation have malodorous properties at concentrations far below those at which toxic effects occur. Although odour annoyance cannot be regarded as an adverse health effect in a strict sense, it does affect the quality of life. Therefore, odour threshold levels have been indicated where relevant and used as a basis for separate guideline values.

For practical purposes, the following characteristics and respective levels were considered in the evaluation of sensory effects:

- intensity, where the *detection threshold level* is defined as the lower limit of the perceived intensity range (by convention the lowest concentration that can be detected in 50% of the cases in which it is present);

- quality, where the *recognition threshold level* is defined as the lowest concentration at which the sensory effect, such as odour, can be recognized correctly in 50% of the cases; and

- acceptability and annoyance, where the *nuisance threshold level* is defined as the concentration at which not more than a small proportion of the population (less than 5%) experiences annoyance for a small part of the time (less than 2%); since annoyance will be influenced by a number of psychological and socioeconomic factors, a nuisance threshold level cannot be defined on the basis of concentration alone.

During revision of the guidelines, the problems of irritation (for example, of the skin) and headache were also considered as possible problems of annoyance. It was agreed that headache should be regarded as a health endpoint and not merely as a matter of annoyance.

CRITERIA FOR CARCINOGENIC ENDPOINT

Cancer risk assessment is basically a two-step procedure, involving a qualitative assessment of how likely it is that an agent is a human carcinogen, and a quantitative assessment of the cancer risk that is likely to occur at given levels and duration of exposure (*11*).

Qualitative assessment of carcinogenicity

The decision to consider a substance as a carcinogen is based on the qualitative evaluation of all available information on carcinogenicity, ensuring that the association is unlikely to be due to chance alone. Here the classification criteria of the International Agency for Research on Cancer (IARC) have been applied (Box 1). In dealing with carcinogens, a "general rule" and exceptions from this were defined. The "general rule" states that for compounds in IARC Groups 1 and 2A (proven human carcinogens, and carcinogens with at least limited evidence of human carcinogenicity), guideline values are derived with the use of quantitative risk assessment with low-dose risk extrapolation. For compounds in Groups 2B (inadequate evidence in humans but sufficient evidence in animals), 3 (unclassifiable as to carcinogenicity in humans) and 4 (noncarcinogenic), guideline values are derived with the use of a threshold (uncertainty factor) method. For compounds in Group 2B, this may incorporate a separate factor for the possibility of a carcinogenic effect in humans.

In case of sufficient scientific evidence, one may be justified in deviating from the "general rule". First, a compound classified in Group 1 or 2A may be assessed with the use of the uncertainty factor methodology, provided that there is strong evidence that it is not genotoxic as judged from a battery of short-term test systems for gene mutation, DNA damage, etc. In such cases it can be established with certainty that an increase in exposure to the compound is associated with an increase in cancer incidence only above a certain level of exposure. It was considered that this required a level of understanding of the mechanisms of action not presently available for the compounds classified as Group 1 or 2A on the current list. Second, a compound in Group 2B may be assessed with the use of quantitative risk assessment methods instead of the uncertainty factor approach. This may be considered appropriate where the mechanism of carcinogenesis in animals is likely to be a non-threshold phenomenon as indicated, for example, by the genotoxic activity of the compound in different short-term test systems.

Quantitative assessment of carcinogenic potency

The aim of quantitative risk assessment is to use information available from very specific study situations to predict the risk to the general population posed by exposure to ambient levels of carcinogens. In general, therefore, quantitative risk assessment includes the extrapolation of risk from relatively high dose levels (characteristic of animal experiments or occupational exposures), where cancer responses can be measured, to relatively low dose levels, which are of concern in environmental protection and where such

Box 1. Classification criteria of the International Agency for Research on Cancer

Group 1 – the agent (mixture) is carcinogenic to humans.
The exposure circumstance entails exposures that are carcinogenic to humans.
This category is used when there is *sufficient evidence* of carcinogenicity in humans. Exceptionally, an agent (mixture) may be placed in this category when evidence in humans is less than sufficient but there is *sufficient evidence* of carcinogenicity in experimental animals and strong evidence in exposed humans that the agent (mixture) acts through a relevant mechanism of carcinogenicity.

Group 2
This category includes agents, mixtures and exposure circumstances for which, at one extreme, the degree of evidence of carcinogenicity in humans is almost sufficient, as well as those for which, at the other extreme, there are no human data but for which there is evidence of carcinogenicity in experimental animals. Agents, mixtures and exposure circumstances are assigned to either group 2A (probably carcinogenic to humans) or group 2B (possibly carcinogenic to humans) on the basis of epidemiological and experimental evidence of carcinogenicity and other relevant data.

Group 2A – the agent (mixture) is probably carcinogenic to humans.
The exposure circumstance entails exposures that are probably carcinogenic to humans.
This category is used when there is *limited evidence* of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. In some cases, an agent (mixture) may be classified in this category when there is inadequate evidence of carcinogenicity in humans and *sufficient evidence* of carcinogenicity in experimental animals and strong evidence that the carcinogenesis is mediated by a mechanism that also operates in humans. Exceptionally, an agent, mixture or exposure circumstance may be classified in this category solely on the basis of limited evidence of carcinogenicity in humans.

Group 2B – the agent (mixture) is possibly carcinogenic to humans.
The exposure circumstance entails exposures that are possibly carcinogenic to humans.
This category is used for agents, mixtures and exposure circumstances for which there is *limited evidence* of carcinogenicity in humans and less than *sufficient evidence of* carcinogenicity in experimental animals. It may also be used when there is *inadequate evidence* of carcinogenicity in humans but there is *sufficient evidence* of carcinogenicity in experimental animals. In some instances, an agent, mixture or exposure circumstance for which there is *inadequate evidence* of carcinogenicity in humans but *limited evidence* of carcinogenicity in experimental animals together with supporting evidence from other relevant data may be placed in this group.

Box 1. (contd)

Group 3 – The agent (mixture or exposure circumstance) is not classifiable as to its carcinogenicity to humans.
This category is used most commonly for agents, mixtures and exposure circumstances for which the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals. Exceptionally, agents (mixtures) for which the evidence of carcinogenicity is inadequate in humans but sufficient in experimental animals may be placed in this category when there is strong evidence that the mechanism of carcinogenicity in experimental animals does not operate in humans. Agents, mixtures and exposure circumstances that do not fall into any other group are also placed in this category.

Group 4 – The agent (mixture) is probably not carcinogenic to humans.
This category is used for agents or mixtures for which there is *evidence suggesting lack of carcinogenicity* in humans and in experimental animals. In some instances, agents or mixtures for which there is *inadequate evidence* of carcinogenicity in humans but *evidence suggesting lack of carcinogenicity* in experimental animals, consistently and strongly supported by a broad range of other relevant data, may be classified in this group.

Source: IARC *(12)*.

risks are too small to be measured directly, either by animal studies or by epidemiological studies.

The choice of the extrapolation model depends on the current understanding of the mechanisms of carcinogenesis *(13)*, and *no* single mathematical procedure can be regarded as fully appropriate for low-dose extrapolation. Methods based on a linear, non-threshold assumption have been used at the national and international level more frequently than models that assume a safe or virtually safe threshold.

In these guidelines, the risk associated with lifetime exposure to a certain concentration of a carcinogen in the air has been estimated by linear extrapolation and the carcinogenic potency expressed as the incremental unit risk estimate. The incremental unit risk estimate for an air pollutant is defined as "the additional lifetime cancer risk occurring in a hypothetical population in which all individuals are exposed continuously from birth throughout their lifetimes to a concentration of 1 μg/m^3 of the agent in the air they breathe" *(14)*.

The results of calculations expressed in unit risk estimates provide the opportunity to compare the carcinogenic potency of different compounds and can help to set priorities in pollution control, taking into account current levels of exposure. By using unit risk estimates, any reference to the "acceptability" of risk is avoided. The decision on the acceptability of a risk should be made by national authorities within the framework of risk management. To support authorities in the decision-making process, the guideline sections for carcinogenic pollutants provide the concentrations in air associated with an excess cancer risk of 1 in a population of 10 000, 1 in 100 000 or 1 in 1 000 000, respectively, calculated from the unit risk.

For those substances for which appropriate human studies are available, the method known as the "average relative risk model" has been used, and is therefore described in more detail below.

Several methods have been used to estimate the incremental risks based on data from animal studies. Two general approaches have been proposed. A strictly linearized estimate has generally been used by the US Environmental Protection Agency (EPA) *(14)*. Nonlinear relations have been proposed for use when the data derived from animal studies indicate a nonlinear dose–response relationship or when there is evidence that the capacity to metabolize the polluting chemical to a carcinogenic form is of limited capacity.

Quantitative assessment of carcinogenicity based on human data

Quantitative assessment using the average relative risk model comprises four steps: (*a*) selection of studies; (*b*) standardized description of study results in terms of relative risk, exposure level and duration of exposure; (*c*) extrapolation towards zero dose; and (*d*) application to a general (hypothetical) population.

First, a reliable human study must be identified, where the exposure of the study population can be estimated with acceptable confidence and the excess cancer incidence is statistically significant. If several studies exist, the best representative study should be selected or several risk estimates evaluated.

Once a study is identified, the relative risk as a measure of response is calculated. It is important to note that the 95% confidence limits around the central estimate of the relative risk can be wide and should be specifically stated and evaluated. The relative risk is then used to calculate the excess lifetime cancer risk expressed as unit risk (UR) associated with a lifetime exposure to 1 μg/m^3, as follows:

$$UR = \frac{P_0(RR - 1)}{X}$$

where: P_0 = background lifetime risk; this is taken from age/cause-specific death or incidence rates found in national vital statistics tables using the life table methodology, or it is available from a matched control population

RR = relative risk, being the ratio between the observed (O) and expected (E) number of cancer cases in the exposed population; the relative risk is sometimes expressed as the standardized mortality ratio SMR = (O/E) × 100

X = lifetime average exposure (standardized lifetime exposure for the study population on a lifetime continuous exposure basis); in the case of occupational studies, X represents a conversion from the occupational 8-hour, 240-day exposure over a specific number of working years and can be calculated as X = 8-hour TWA × 8/24 × 240/365 × (average exposure duration [in years])/(life expectancy [70 years]), where TWA is the time-weighted average (μg/m^3).

It should be noted that the unit lifetime risk depends on P_0 (background lifetime risk), which is determined from national age-specific cancer incidence or mortality rates. Since these rates are also determined by exposures other than the one of interest and may vary from country to country, it follows that the UR may also vary from one country to another.

Necessary assumptions for average relative risk method

Before any attempt is made to assess the risk in the general population, numerous assumptions are needed at each phase of the risk assessment process to fill in various gaps in the underlying scientific database. As a first step in any given risk assessment, therefore, an attempt should be made to identify the major assumptions that have to be made, indicating their probable consequences. These assumptions are as follows.

1. *The response (measured as relative risk) is some function of cumulative dose or exposure.*

2. *There is no threshold dose for carcinogens.*

Many stages in the basic mechanism of carcinogenesis are not yet known or are only partly understood. Taking available scientific findings into consideration,

however, several scientific bodies *(8, 15–17)* have concluded that there is no scientific basis for assuming a threshold or no-effect level for chemical carcinogens. This view is based on the fact that most agents that cause cancer also cause irreversible damage to deoxyribonucleic acid (DNA). The assumption applies for all non-threshold models.

3. *The linear extrapolation of the dose–response curve towards zero gives an upper-bound conservative estimate of the true risk function if the unknown (true) dose–response curve has a sigmoidal shape.*
The scientific justification for the use of a linear non-threshold extrapolation model stems from several sources: the similarity between carcinogenesis and mutagenesis as processes that both have DNA as target molecules; the strong evidence of the linearity of dose–response relationships for mutagenesis; the evidence for the linearity of the DNA binding of chemical carcinogens in the liver and skin; the evidence for the linearity in the dose–response relationship in the initiation stage of the mouse 2-stage tumorigenesis model; and the rough consistency with the linearity of the dose–response relationships for several epidemiological studies. This assumption applies for all linear models.

4. *There is constancy of the relative risk in the specific study situation.*
In a strict sense, constancy of the relative risk means that the background age/cause-specific rate at any time is increased by a constant factor. The advantage of the average relative risk method is that this needs to be true only for the average.

Advantages of the method

The average relative risk method was selected in preference to many other more sophisticated extrapolation models because it has several advantages, the main one being that it seems to be appropriate for a fairly large class of different carcinogens, as well as for different human studies. This is possible because averaging doses, that is, averaging done over concentration and duration of exposure, gives a reasonable measure of exposure when dose rates are not constant in time. This may be illustrated by the fact that the use of more sophisticated models *(14, 18, 19)* results in risk estimates very similar to those obtained by the average relative risk method.

Another advantage of the method is that the carcinogenic potency can be calculated when estimates of the average level and duration of exposure are the only known parameters besides the relative risk. Furthermore, the method has the advantage of being simple to apply, allowing non-experts in the field of risk models to calculate a lifetime risk from exposure to the carcinogens.

Limitations of the method

As pointed out earlier, the average relative risk method is based on several assumptions that appear to be valid in a wide variety of situations. There are specific situations, however, in which the method cannot be recommended, mainly because the assumptions do not hold true.

The cumulative dose concept, for instance, is inappropriate when the mechanism of the carcinogen suggests that it cannot produce cancer throughout all stages of the cancer development process. Also, specific toxicokinetic properties, such as a higher excretion rate of a carcinogen at higher doses or a relatively lower production rate of carcinogenic metabolites at lower doses, may diminish the usefulness of the method in estimating cancer risk. Furthermore, supralinearity of the dose–response curve or irregular variations in the relative risk over time that cannot be eliminated would reduce the value of the model. Nevertheless, evidence concerning these limitations either does not exist or is still too preliminary to make the average relative risk method inappropriate for carcinogens evaluated here.

A factor of uncertainty, rather than of methodological limitation, is that data on past exposure are nearly always incomplete. Although it is generally assumed that in the majority of studies the historical dose rate can be determined within an order of magnitude, there are possibly greater uncertainties, even of more than two orders of magnitude, in some studies. In the risk assessment process it is of crucial importance that this degree of uncertainty be clearly stated. This is often done simply by citing upper and lower limits of risk estimates. Duration of exposure and the age- and time-dependence of cancer caused by a particular substance are less uncertain parameters, although the mechanisms of relationship are not so well understood *(11)*.

Risk estimates from animal cancer bioassays

Animal bioassays of chemicals provide important information on the human risk of cancer from exposure to chemicals. These data enhance our confidence in assessing human cancer risks on the basis of epidemiological data.

There is little doubt of the importance of animal bioassay data in reaching an informed decision on the carcinogenic potential of a chemical. The collection and use of data such as those on saturation mechanisms, absorption, distribution and metabolic pathways, as well as on interaction with other chemicals, is important and should be continued. Regrettably, these data were not always available for the air pollutants evaluated during the update and revision of the guidelines. The process of evaluating guidelines

and the impact of exposure to these chemicals on human health should continue and be revised as new information becomes available.

Several chemicals considered in this publication have been studied using animal cancer bioassays. The process is continuing and new information on the potential carcinogenicity of chemicals is rapidly appearing. Consequently, the status of chemicals is constantly being reassessed.

There is no clear consensus on appropriate methodology for the risk assessment of chemicals for which the critical effect may not have a threshold, such as genotoxic carcinogens and germ cell mutagens. A number of approaches based largely on characterization of dose–response have been adopted for assessment of such effects:

- quantitative extrapolation by mathematical modelling of the dose–response curve to estimate the risk at likely human intakes or exposures (low-dose risk extrapolation);
- relative ranking of potencies in the experimental range; and
- division of effect levels by an uncertainty factor.

Low-dose risk extrapolation has been accomplished by the use of mathematical models such as the Armitage-Doll multi-stage model. In more recently developed biological models, the different stages in the process of carcinogenesis have been incorporated and time to tumour has been taken into account *(20)*. In some cases, such as that of butadiene, uncertainty regarding the metabolism in humans and experimental animals precluded the choice of the appropriate animal model for low-dose risk extrapolation. In other cases where data permitted, attempts were made to incorporate the dose delivered to the target tissue into the dose–response analysis (physiologically based pharmacokinetic modelling).

During revision of the guidelines, other approaches to establishing guideline levels for carcinogens were considered. Such approaches involve the identification of a level of exposure at which the risk is known to be small and the application of uncertainty factors to derive a level of exposure at which the risk is accepted as being exceedingly small or negligible. This approach has been adopted in the United Kingdom, for example. It was agreed that such an approach might be applicable on a national or smaller scale, but that it was unlikely to be generally applicable.

Interpretation of risk estimates

The risk estimates presented in this book should *not* be regarded as being equivalent to the true cancer risk. It should be noted that crude expression

of risk in terms of excess incidence or numbers of cancers per unit of the population at doses or concentrations much less than those on which the estimates are based may be inappropriate, owing to the uncertainties of quantitative extrapolation over several orders of magnitude. Estimated risks are believed to represent only the plausible upper bounds, and may vary widely depending on the assumptions on which they are based.

The presented quantitative risk estimates can provide policy-makers with rough estimates of risk that may serve well as a basis for setting priorities, balancing risks and benefits, and establishing the degree of urgency of public health problems among subpopulations inadvertently exposed to carcinogens. A risk management approach for compounds for which the critical effect is considered not to have a threshold involves eliminating or reducing exposure as far as practically or technologically possible. Characterization of the dose–response, as indicated in the procedures described above, can be used in conjunction with this approach to assess the need to reduce exposure.

Combined exposures

Exposure to combinations of air pollutants is inevitable. Data dealing with the effects of co-exposure to air pollutants are, however, very limited and it is not possible to recommend guidelines for such combinations. Of course, measures taken to control air pollution frequently lead to the reduction in concentrations of more than one pollutant. This is often achieved by controlling sources of pollutants rather than by focusing on individual pollutants.

ECOLOGICAL EFFECTS

The importance of taking an integrated view of both health and ecological effects in air quality management was recognized from the beginning of the project. Ecological effects may have a significant indirect influence on human health and wellbeing. For example, most of the major urban air pollutants are known to have adverse effects at low levels on plants, including food crops. A consultation group was therefore convened to consider the ecological effects on terrestrial vegetation of sulfur dioxide, nitrogen dioxide, and ozone and other photochemical oxidants. These substances are important both because of the high anthropogenic amounts produced and because of their wide distribution. They deserve special attention because of significant adverse effects on ecological systems in concentrations far below those known to be harmful to humans.

The pollutants selected for consideration here form only part of the vast range of air pollutants that have ecological effects. The project timetable

permitted only an evaluation of adverse effects on terrestrial plant life, although effects on animal and aquatic ecosystems are also of great concern in parts of Europe. Nevertheless, even this limited evaluation clearly indicates the importance attached to the ecological effects of such pollutants in the European Region.

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Summary of the guidelines

The term "guidelines" in the context of this book implies not only numerical values (guideline values), but also any kind of guidance given. Accordingly, for some substances the guidelines encompass recommendations of a more general nature that will help to reduce human exposure to harmful levels of air pollutants. For some pollutants no guideline values are recommended, but risk estimates are indicated instead.

The numerical guideline values and the risk estimates for carcinogens (Tables 2–4) should be regarded as the shortest possible summary of a complex scientific evaluation process. Nevertheless, the information given in the tables should not be used without reference to the rationale given in the chapters on the respective pollutants. Scientific results are an abstraction of real situations, and this is even more true for numerical values and risk estimates based on such results. Numerical guideline values, therefore, are not to be regarded as separating the acceptable from the unacceptable, but rather as indications. They are proposed in order to help avoid major discrepancies in reaching the goal of effective protection against recognized hazards for human health and the environment. Moreover, numerical

Table 2. Guideline values for individual substances based on effects other than cancer or odour/annoyance

Substance	Time-weighted average	Averaging time
Cadmium	5 ng/m^3[a]	annual
Carbon disulfide[b]	100 µg/m^3	24 hours
Carbon monoxide	100 mg/m^3[c]	15 minutes
	60 mg/m^3[c]	30 minutes
	30 mg/m^3[c]	1 hour
	10 mg/m^3	8 hours
1,2-Dichloroethane[b]	0.7 mg/m^3	24 hours
Dichloromethane	3 mg/m^3	24 hours
	0.45 mg/m^3	1 week

Table 2 (contd)

Substance	Time-weighted average	Averaging time
Fluoride[d]	—	—
Formaldehyde	0.1 mg/m^3	30 minutes
Hydrogen sulfide[b]	150 µg/m^3	24 hours
Lead	0.5 µg/m^3	annual
Manganese	0.15 µg/m^3	annual
Mercury	1 µg/m^3	annual
Nitrogen dioxide	200 µg/m^3	1 hour
	40 µg/m^3	annual
Ozone	120 µg/m^3	8 hours
Particulate matter[e]	Dose–response	—
Platinum[f]	—	—
PCBs[g]	—	—
PCDDs/PCDFs[h]	—	—
Styrene	0.26 mg/m^3	1 week
Sulfur dioxide	500 µg/m^3	10 minutes
	125 µg/m^3	24 hours
	50 µg/m^3	annual
Tetrachloroethylene	0.25 mg/m^3	annual
Toluene	0.26 mg/m^3	1 week
Vanadium[b]	1 µg/m^3	24 hours

[a] The guideline value is based on the prevention of a further increase of cadmium in agricultural soils, which is likely to increase the dietary intake.

[b] Not re-evaluated for the second edition of the guidelines.

[c] Exposure at these concentrations should be for no longer than the indicated times and should not be repeated within 8 hours.

[d] Because there is no evidence that atmospheric deposition of fluorides results in significant exposure through other routes than air, it was recognized that levels below 1 µg/m^3, which is needed to protect plants and livestock, will also sufficiently protect human health.

[e] The available information for short- and long-term exposure to PM_{10} and $PM_{2.5}$ does not allow a judgement to be made regarding concentrations below which no effects would be expected. For this reason no guideline values have been recommended, but instead risk estimates have been provided (see Chapter 7, Part 3).

[f] It is unlikely that the general population, exposed to platinum concentrations in ambient air at least three orders of magnitude below occupational levels where effects were seen, may develop similar effects. No specific guideline value has therefore been recommended.

[g] No guideline value has been recommended for PCBs because inhalation constitutes only a small proportion (about 1–2%) of the daily intake from food.

[h] No guideline value has been recommended for PCDDs/PCDFs because inhalation constitutes only a small proportion (generally less than 5%) of the daily intake from food.

guidelines for different substances are not directly comparable. Variations in the quality and extent of the scientific information and in the nature of critical effects, although usually reflected in the applied uncertainty factor, result in guideline values that are only to a limited extent comparable between pollutants.

Owing to the different bases for evaluation, the numerical values for the various air pollutants should be considered in the context of the accompanying scientific documentation giving the derivation and scientific considerations. Any *isolated* interpretation of numerical data should therefore be avoided, and guideline values should be used and interpreted in conjunction with the information contained in the appropriate sections.

It is important to note that the approach taken in the preparation of the guidelines was to evaluate data on the health effects of individual compounds. Consequently, each chemical was considered in isolation. Pollutant mixtures can yield different toxic effects, but data are at present insufficient for guidelines relating to mixtures to be laid down. There is little emphasis on interaction between pollutants that might lead to additive or synergistic effects and on the environmental fate of pollutants, though there is growing evidence about the role of solvents in atmospheric photochemical processes leading to the formation or degradation of ozone, the formation of acid rain, and the propensity of metals and trace elements to accumulate in environmental niches. These factors militate strongly against allowing a rise in ambient pollutant levels. Many uncertainties still remain, particularly regarding the ecological effects of pollutants, and therefore efforts should be continued to maintain air quality at the best possible level.

GUIDELINE VALUES BASED ON NON-CANCER EFFECTS OTHER THAN CANCER

The guideline values for individual substances based on effects other than cancer and annoyance from odour are given in Table 2. The emphasis in the guidelines is placed on exposure, since this is the element that can be controlled to lessen dose and hence lessen the consequent health effect. When general ambient air levels are orders of magnitude lower than the guideline values, present exposures are unlikely to cause concern. Guideline values in those cases are directed only to specific release episodes or specific indoor pollution problems.

As stated earlier, the starting point for the derivation of guideline values was to define the lowest concentration at which adverse effects are observed. On

the basis of the body of scientific evidence and judgements of uncertainty factors, numerical guideline values were established to the extent possible. Compliance with the guideline values does not, however, guarantee the absolute exclusion of undesired effects at levels below the guideline values. It means only that guideline values have been established in the light of current knowledge and that uncertainty factors based on the best scientific judgements have been incorporated, though some uncertainty cannot be avoided.

For some of the substances, a direct relationship between concentrations in air and possible toxic effects is very difficult to establish. This is especially true of those pollutants for which a greater body burden results from ingestion than from inhalation. For instance, available data show that for the general population the food chain is the critical route of non-occupational exposure to lead and cadmium, and to persistent organic pollutants such as dioxins and PCBs. On the other hand, emissions of these pollutants into air may contribute significantly to the contamination of food by these compounds. Complications of this kind were taken into consideration, and an attempt was made to develop guidelines that would also prevent those toxic effects of air pollutants that resulted from uptake by both ingestion and inhalation.

For certain compounds, such as organic solvents, the proposed health-related guidelines are orders of magnitude higher than current ambient levels. The fact that existing environmental levels for some substances are much lower than the guideline levels by no means implies that pollutant burdens may be increased up to the guideline values. Any level of air pollution is a matter of concern, and the existence of guideline values never means a licence to pollute.

Unfortunately, the situation with regard to actual environmental levels and proposed guideline values for some substances is just the opposite – guideline values are below existing levels in some parts of Europe. For instance, the guideline values recommended for major urban air pollutants such as nitrogen dioxide, ozone and sulfur dioxide point to the need for a significant reduction of emissions in some areas.

For substances with malodorous properties at concentrations below those where toxic effects occur, guideline values likely to protect the public from odour nuisance were established; these were based on data provided by expert panels and field studies (Table 3). In contrast to other air pollutants, odorous substances in ambient air often cannot be determined easily and

Table 3. Rationale and guideline values based on sensory effects or annoyance reactions, using an averaging time of 30 minutes

Substance	Detection threshold	Recognition threshold	Guideline value
Carbon disulfide[a] (index substance for viscose emissions)	200 µg/m^3	—	20 µg/m^3
Hydrogen sulfide[a]	0.2–2.0 µg/m^3	0.6–6.0 µg/m^3	7 µg/m^3
Formaldehyde	0.03–0.6 mg/m^3	—	0.1 mg/m^3
Styrene	70 µg/m^3	210–280 µg/m^3	70 µg/m^3
Tetrachloroethylene	8 mg/m^3	24–32 mg/m^3	8 mg/m^3
Toluene	1 mg/m^3	10 mg/m^3	1 mg/m^3

[a] Not re-evaluated for the second edition of the guidelines.

systematically by analytical methods because the concentrations are usually very low. Furthermore, odours in the ambient air frequently result from a complex mixture of substances and it is difficult to identify individual ones; future work may have to concentrate on odours as perceived by individuals rather than on separate odorous substances.

GUIDELINES BASED ON CARCINOGENIC EFFECTS

In establishing criteria upon which guidelines could be based, it became apparent that carcinogens and noncarcinogens would require different approaches. These approaches are determined by theories of carcinogenesis, which postulate that there is no threshold for effects (that is, that there is no safe level). Risk managers are therefore faced with two choices: either to prohibit a chemical or to regulate it at levels that result in an acceptable degree of risk. Indicative figures for risk and exposure assist the risk manager to reach the latter decision. Air quality guidelines are therefore indicated in terms of incremental unit risks (Table 4) in respect of those carcinogens that are considered to be genotoxic (see Chapter 2). To allow risk managers to judge the acceptability of risks, this edition of the guidelines has provided concentrations of carcinogenic air pollutants associated with an excess lifetime cancer risk of 1 per 10 000, 1 per 100 000 and 1 per 1 000 000.

For butadiene, there is substantial information on its mutagenic and carcinogenic activity. It has been shown that butadiene is mutagenic in both

Table 4. Carcinogenic risk estimates based on human studies[a]

Substance	IARC Group	Unit risk[b]	Site of tumour
Acrylonitrile[c]	2A	2×10^{-5}	lung
Arsenic	1	1.5×10^{-3}	lung
Benzene	1	6×10^{-6}	blood (leukaemia)
Butadiene	2A	—	multisite
Chromium (VI)	1	4×10^{-2}	lung
Nickel compounds	1	4×10^{-4}	lung
Polycyclic aromatic hydrocarbons (BaP)[d]	—	9×10^{-2}	lung
Refractory ceramic fibres	2B	1×10^{-6} (fibre/l)$^{-1}$	lung
Trichloroethylene	2A	4.3×10^{-7}	lung, testis
Vinyl chloride[c]	1	1×10^{-6}	liver and other sites

[a] Calculated with average relative risk model.

[b] Cancer risk estimates for lifetime exposure to a concentration of 1 µg/m^3.

[c] Not re-evaluated for the second edition of the guidelines.

[d] Expressed as benzo[*a*]pyrene (based on a benzo[*a*]pyrene concentration of 1 µg/m^3 in air as a component of benzene-soluble coke-oven emissions).

bacterial and mammalian systems, but metabolic activation into DNA-reactive metabolites is required for this activity. In general, metabolism of butadiene to epoxides in humans is significantly less than in mice and rats, with mice having the highest metabolic activity. Human cancer risk estimates for butadiene based on bioassays vary considerably depending on the animal species used, with risk estimates based on data in mice being 2–3 orders of magnitude higher than those based on rat data. At present, no definite conclusion can be made as to which animal species is most appropriate for human cancer risk estimates, and thus no guideline value is recommended for butadiene.

Separate consideration is given to risk estimates for asbestos (Table 5) and radon daughters (Table 6) because they refer to different physical units, and the risk estimates are indicated in the form of ranges.

Risk estimation for residential radon exposure has often been based on extrapolation of findings in underground miners. Several circumstances, however, make such estimates uncertain for the general population: exposure to other factors in the mines; differences in age and sex; size distribution of aerosols; the attached fraction of radon progeny; breathing rate; and

Table 5. Risk estimates for asbestos		
Concentration	**Range of lifetime risk estimates**	
500 F*/m^3 (0.0005 F/ml)[a]	10^{-6}–10^{-5}	(lung cancer in a population where 30% are smokers)
	10^{-5}–10^{-4}	(mesothelioma)

[a] F* = fibres measured by optical methods.

Table 6. Risk estimates and recommended action level for radon progeny		
Exposure	**Lung cancer excess lifetime risk estimate**	**Recommended level for remedial action in buildings**
1 Bq/m^3	$3–6 \times 10^{-5}$	$\geq$ 100 Bq/m^3 (annual average)

route. Furthermore, uncertainties in the exposure–response exist, and possible differences in the relative risk estimates for smokers and non-smokers are not fully understood (see Chapter 8, Part 3).

For radon, a unit risk of approximately $3–6 \times 10^{-5}$ per Bq/m^3 can be calculated assuming a life time risk of lung cancer of 3% (Table 6). This means that a person living in an average European house with 50 Bq/m^3 has a lifetime excess lung cancer risk of $1.5–3 \times 10^{-3}$ Thus current levels of radon in dwellings and other buildings are of public health concern. In addition it should be noted that a lifetime lung cancer risk below about 10^{-4} could normally not be expected to be achievable because natural concentration of radon in ambient air outdoors is about 10 Bq/m^3. Therefore no numerical guideline value for radon is recommended.

It is important to note that quantitative risk estimates may give an impression of accuracy that they do not in fact have. An excess of cancer in a population is a biological effect and not a mathematical function, and uncertainties of risk estimation are caused not only by inadequate exposure data but also, for instance, by the fact that specific metabolic properties of agents are not reflected in the models. The guidelines do not indicate therefore that a specified lifetime risk is virtually safe or acceptable.

The decision on the acceptability of a certain risk should be taken by the national authorities in the context of a broader risk management process. Risk estimate figures should not be applied in isolation when regulatory decisions are being made; combined with data on exposure levels and individuals exposed, they may be a useful contribution to risk assessment. Risk

assessment can then be used together with technological, economic and other considerations in the risk management process.

GUIDELINES BASED ON EFFECTS ON VEGETATION

Although the main objective of the air quality guidelines is the direct protection of human health, it was decided that ecological effects of air pollutants on vegetation should also be considered. The effects of air pollutants on the natural environment are of special concern when they occur at concentrations lower than those that damage human health. In such cases, air quality guidelines based only on effects on human health would not allow for environmental damage that might indirectly affect human wellbeing.

Ecologically based guidelines for preventing adverse effects on terrestrial vegetation were included in the first edition of this book, and guidelines were recommended for some gaseous air pollutants. Since that time, however, significant advances in the scientific understanding of the impacts of air pollutants on the environment have been made. For the updating and revision of the guidelines, the ecological effects of major air pollutants were considered in more detail within the framework of the Convention on Long-range Transboundary Air Pollution. This capitalizes on the scientific work undertaken since 1988 to formulate criteria for the assessment of the effects of air pollutants on the natural environment, such as critical levels and critical loads.

It should be understood that the pollutants selected (SO_2, NO_x and ozone/photochemical oxidants) (Table 7) are only a few of a larger category of air

Table 7. Guideline values for individual substances based on effects on terrestrial vegetation

Substance	Guideline value	Averaging time
SO_2: critical level	10–30 µg/m^3 [a]	annual
critical load	250–1500 eq/ha/year[b]	annual
NO_x: critical level	30 µg/m^3	annual
critical load	5–35 kg N/ha/year[b]	annual
Ozone: critical level	0.2–10 ppm·h[a, c]	5 days–6 months

[a] Depending on the type of vegetation (see Part III).

[b] Depending on the type of soil and ecosystem (see Part III).

[c] AOT: Accumulated exposure Over a Threshold of 40 ppb.

pollutants that may adversely affect the ecosystem, and that the effects considered are only part of the spectrum of ecological effects. Effects on aquatic ecosystems were not evaluated, nor were effects on animals taken into account. Nevertheless, the available information indicates the importance of these pollutants and of their effects on terrestrial vegetation in the European Region.

CHAPTER 4

Use of the guidelines in protecting public health

When strategies to protect public health are under consideration, the air quality guidelines need to be placed in the perspective of total chemical exposure. The interaction of humans and the biosphere is complex. Individuals can be exposed briefly or throughout their lifetime to chemicals in air, water and food; exposures may be environmental and occupational. In addition, individuals vary widely in their response to exposure to chemicals; each person has a pre-existing status (for example, age, sex, pregnancy, pulmonary disease, cardiovascular disease, genetic make-up) and a lifestyle, in which such factors as exercise and nutrition play key roles. All these different elements may influence a person's susceptibility to chemicals. Various sensitivities also exist within the plant kingdom and need to be considered in protecting the environment.

The primary aim of these guidelines is to provide a uniform basis for the protection of public health and of ecosystems from adverse effects of air pollution, and to eliminate or reduce to a minimum exposure to those pollutants that are known or are likely to be hazardous. The guidelines are based on the scientific knowledge available at the time of their development. They have the character of recommendations, and it is not intended or recommended that they simply be adopted as standards. Nevertheless, countries may wish to transform the recommended guidelines into legally enforceable standards, and this chapter discusses ways in which this may be done. It is based on the report of a WHO working group (*1*). The discussion is limited to ambient air and does not include the setting of emission standards.

In the process of moving from a "guideline" or a "guideline value" to a "standard", a number of factors beyond the exposure–response relationship need to be taken into account. These factors include current concentrations of pollutants and exposure levels of a population, the specific mixture of air pollutants, and the specific social, economic and cultural conditions encountered. In addition, the standard-setting procedure may be influenced by the likelihood of implementing the standard. These considerations may lead to a standard above or below the respective guideline value.

DEFINITIONS

Several terms are in use to describe the tools available to manage ambient air pollution. To avoid confusion, definitions are needed for the terms used here – guideline, guideline value and standard – within this specific context.

Guideline

A guideline is defined as any kind of recommendation or guidance on the protection of human beings or receptors in the environment from adverse effects of air pollutants. As such, a guideline is not restricted to a numerical value but might also be expressed in a different way, for example as exposure–response information or as a unit risk estimate.

Guideline value

A guideline value is a particular form of guideline. It has a numerical value expressed either as a concentration in ambient air or as a deposition level, which is linked to an averaging time. In the case of human health, the guideline value provides a concentration below which no adverse effects or (in the case of odorous compounds), no nuisance or indirect health significance are expected, although it does not guarantee the absolute exclusion of effects at concentrations below the given value.

Standard

A standard is considered to be the level of an air pollutant, such as a concentration or a deposition level, that is adopted by a regulatory authority as enforceable. Unlike the case of a guideline value, a number of elements in addition to the effect-based level and the averaging time have to be specified in the formulation of a standard. These elements include:

- the measurement strategy
- the data handling procedures
- the statistics used to derive the value to be compared with the standard.

The numerical value of a standard may also include the permitted number of exceedings.

MOVING FROM GUIDELINES TO STANDARDS

The regulatory approach to controlling air pollution differs from country to country. Different countries have different political, regulatory and administrative approaches, and legislative and executive activities can be carried out at various levels such as national, regional and local. Fully effective air quality management requires a framework that guarantees a consistent

derivation of air quality standards and provides a transparent basis for decisions with regard to risk-reducing measures and abatement strategies. In establishing such a framework, several issues should be considered, such as legal aspects, the protection of specific populations at risk, the role of stakeholders in the process, cost–benefit analysis, and control and enforcement measures.

Legal aspects

In setting air quality standards at the national or supranational level, a legislative framework usually provides the basis for the evaluation and decision-making process. The setting of standards strongly depends on the type of risk management strategy adopted. Such a strategy is influenced by country-specific sociopolitical considerations and/or supranational agreements.

Legislation and the format of air quality standards vary from country to country, but in general the following issues should be considered:

- identification and selection of pollutants to which the legislative instrument will apply;
- the process for making decisions about the appropriate standards;
- the numerical value of the standards for the various pollutants, applicable detection methods and monitoring methodology;
- actions to be taken to implement the standard, such as the definition of the time frame needed/allowed for achieving compliance with the standard, considering emission control measures and necessary abatement strategies; and
- identification of responsible enforcement authorities.

Depending on their position within a legislative framework, standards may or may not be legally binding. In some countries the national constitution contains provisions for the protection of public health and the environment. In general, the development of a legal framework on the basis of constitutional provisions comprises two regulatory actions. The first is the enactment of a formal legal instrument, such as an act, a law, an ordinance or a decree, and the second is the development of regulations, by-laws, rules and orders.

Air quality standards may be based solely on scientific and technical data on public health and environmental effects, but other aspects such as cost–benefit or cost–effectiveness may be also taken into consideration. In practice, there are generally several opportunities within a legal framework to

address these economic aspects as well as other issues, such as technical feasibility, structural measures and sociopolitical considerations. These can be taken into account during the standard-setting procedure or at the level of designing appropriate measures to control emissions. This rather complicated process might result in several standards being set, such as an effect-oriented standard as a long-term goal and less stringent interim standards to be achieved within shorter periods of time.

Standards also depend on political choices as to which receptors in the environment should be protected and to what extent. Some countries have separate standards for the protection of public health and the environment. Moreover, the stringency of a standard can be influenced by provisions designed to take account of higher sensitivities of specific receptor groups, such as young children, sick or elderly people, or pregnant women. It might also be important to specify whether effects are considered for individual pollutants or for a combined exposure to several pollutants.

Air quality standards can set the reference point for emission control and abatement strategies on a national level. It should be recognized, however, that exposure to some pollutants is the result of long-range transboundary transport. In these cases adequate protection measures can only be achieved by appropriate international agreements.

Air quality standards should be regularly reviewed, and need to be revised as new scientific evidence on effects on public health and the environment emerges.

Standards often strongly influence the implementation of an air pollution control policy. In many countries, the exceeding of standards is linked to an obligation to develop action plans at the local, regional or national level to reduce air pollution levels. Such plans often address several pollution sources. Standards also play a role in environmental impact assessment procedures and in the provision of public information on the state of the environment. Provisions for such activities can be found in many national legal instruments.

Within national or supranational legislative procedures, the role of stakeholders in the process of standard-setting also needs to be considered. This is dealt with in more detail below.

Items to be considered in setting standards

Within established legal frameworks and using air quality guidelines as a starting point, development of standards involves consideration of a number

of issues. These are in part determined by characteristics of populations or physical properties of the environment. A number of these issues are discussed below.

Adverse health effects

In setting a standard for the control of an environmental pollutant, the effects that the population is to be protected against need to be defined. A hierarchy of effects on health can be identified, ranging from acute illness and death through chronic and lingering diseases and minor and temporary ailments, to temporary physiological or psychological changes. The distinction between adverse and non-adverse effects poses considerable difficulties. Of course, more serious effects are generally accepted as adverse. As one considers effects that are either temporary and reversible, or involve biochemical or functional changes whose clinical significance is uncertain, judgements must be made as to which of these less serious effects should be considered adverse. With any definition of adversity, a significant degree of subjectivity and uncertainty remains. Judgements as to adversity may differ between countries because of factors such as different cultural backgrounds and different background levels of health status.

In some cases, the use of biomarkers or other indicators of exposure may provide a basis for standard-setting. Changes in such indicators, while not necessarily being adverse in themselves, may be predictors of significant effects on health. For example, the blood lead concentration can provide information on the likelihood of impairment of neurobehavioural development.

Special populations at risk

Sensitive populations or groups are defined here as those impaired by concurrent disease or other physiological limitations, and those with specific characteristics that make the health consequences of exposure more significant (such as the developmental phase in children or reduction in reserve capacity in the elderly). In addition, other groups may be judged to be at special risk because of their exposure patterns or due to an increased effective dose for a given exposure. Sensitive populations may vary from country to country owing to differences in the number of people lacking access to adequate medical care, in the existence of endemic disease, in the prevailing genetic factors, or in the prevalence of debilitating diseases, nutritional deficiencies or lifestyle factors. It is up to the politician to decide which specific groups at risk should be protected by the standards (and thus which should not be protected).

Exposure–response relationships

A key factor to be considered in developing standards is information about the exposure–response relationship for the pollutant concerned. For a number of pollutants an attempt has been made to provide exposure–response relationships in the revised version of the guidelines. For particulate matter and ozone, detailed tables specifying the exposure–response relationship are provided. The information included in these tables is derived from epidemiological studies of the effects of these pollutants on health. Such information is available for only a few of the pollutants considered in the guidelines. For known "no-threshold compounds" such as the carcinogen benzene, quantitative risk assessment methods provide estimates of risk at different exposure concentrations.

When developing standards, regulators should consider the degree of uncertainty about exposure–response relationships provided in the guidelines. Differences in the population structure, climate and geography that can have an impact on the prevalence, frequency and severity of effects may modify the exposure–response relationships provided in the guidelines.

Exposure characterization

An important factor to be considered in developing standards is that of how many people are exposed to concentrations of concern and the distribution of exposure among various population groups. Current distributions of exposure should be considered, together with those that are likely to occur should the standard be met. Besides using monitoring data, results of exposure modelling can be used at this stage. The origins of pollutants, including long-range transport and its contribution to ambient levels, should also be evaluated.

The extent to which ambient air quality estimates from monitoring networks or models correspond to personal exposure in the population is also a factor to be considered in the standard-setting. This will depend on the pollutant in question (for example, personal exposure to carbon monoxide is poorly characterized by fixed-site monitors) as well as on a number of local characteristics, including lifestyle, climatic conditions, spatial distribution of pollution sources and local determinants of pollution dispersion.

Other important exposure-related concerns include:

- how much of total human exposure is due to ambient, outdoor sources as opposed to indoor sources; and

- where multiple routes of exposure are important, how to apportion the regulatory burden among the different routes of exposure (such as lead from air sources versus lead from paint, water pipes, etc.).

These factors may vary substantially across countries. For example, indoor air pollution levels might be quite substantial in countries in which fossil and/or biomass fuels are used in homes.

Risk assessment

In general, the central question in developing air quality standards to protect public health or ecosystems is the degree of protection associated with different pollution levels at which standards might be established. In the framework of quantitative risk assessment, various proposals for standards can be considered in health or ecological risk models. These models provide a tool that is increasingly used to inform decision-makers about some of the possible consequences associated with various options for standards, or the reduction in adverse effects associated with moving from the current situation to a particular standard.

The first two steps in risk assessment, namely hazard identification and, in some cases, development of exposure–response relationships, have been provided in these guidelines and are discussed in greater detail in later chapters. The third step, exposure analysis, predicts changes in exposure associated with reductions in emissions from a specific source or groups of sources under different control scenarios. Instead of exposure estimates, ambient concentrations (based on monitoring or modelling) are often used as the inputs to a risk assessment. This is in part because of the availability of information on concentration–response relationships from epidemiological studies in which fixed-site monitors were used.

The final step in a regulatory risk assessment is the risk characterization stage, whereby exposure estimates are combined with exposure–response relationships to generate quantitative estimates of risk (such as how many individuals may be affected). Regulatory risk assessments are likely to result in different risk estimates across countries, owing to differences in exposure patterns and in the size and characteristics of sensitive populations and those at special risk.

It is important to recognize that there are many uncertainties at each stage of a regulatory risk assessment. The results of sensitivity and uncertainty analyses should be presented so as to characterize the impact of major

uncertainties on the risk estimates. In addition, the methods used to conduct the risk assessments should be clearly described and the limitations and caveats associated with the analysis should be discussed.

Acceptability of risk

The role of a regulatory risk assessment in developing standards may differ from country to country, owing to differences in the legal framework and availability of information. Also, the degree of acceptability of risk may vary between countries because of differences in social norms, degree of adversity and risk perception among the general population and various stakeholders. How the risks associated with air pollution compare with those from other pollution sources or human activities may also influence risk acceptability.

In the absence of clearly identified thresholds for health effects for some pollutants, the selection of a standard that provides adequate protection of public health requires an exercise of informed judgement by the regulator. The acceptability of the risks and, therefore, the standard selected will depend on the effect, on the expected incidence and severity of the potential effects, on the size of the population at risk, and on the degree of scientific certainty that the effects will occur at any given level of pollution. For example, if a suspected health effect is severe and the size of the population at risk is large, a more cautious approach would be appropriate than if the effect were less troubling or if the exposed population were small.

Cost–benefit analysis

Two comprehensive techniques provide a framework for comparing monetarized costs and benefits of implementing legislation or policy: cost–effectiveness analysis and cost–benefit analysis. These two techniques differ in their treatment of benefits. In cost–benefit analysis, costs and benefits (for example, avoided harm, injury or damage) of implemented control measures are compared using monetary values. In cost–effectiveness analysis, the costs of control measures are reported in quantitative terms, such as cost per ton of pollutant or cost per exposure unit. That is, the benefits are described in their own physical, chemical or biological terms, such as reduced concentrations or emissions, or avoided cases of illness, crop losses or damage to ecosystems.

Analysis of control measures to reduce ambient pollutant levels

Control measures to reduce emissions of many air pollutants are known. Direct control measures at the source are readily expressed in monetary terms. Indirect control measures, such as alternative traffic plans or changes

in public behaviour, may not all be measurable in monetary terms but their impact should be understood. Effective control measures should be designed to deal with secondary as well as primary pollutants.

Cost identification should include costs of investment, operation and maintenance, both for the present and for the future. Unforeseen effects, technical innovations and developments, and indirect costs arising during implementation of the regulation are additional complicating factors. Cost estimates derived in one geographical area may not be generally transferable to other areas.

Air quality assessment has to provide information about expected air quality, both with and without implementation of control measures. Typically, the assessment will be based on a combination of air quality monitoring data and dispersion modelling. These two assessment methods are complementary, and must be seen as equally important inputs to the assessment process.

For the assessment, several types of data have to be acquired:

- measured concentrations for relevant averaging times (hourly, daily, seasonal) with information on site classification;
- emission data from all significant sources, including emission conditions (such as stack height) and with sufficient information on spatial and temporal variation; and
- meteorological and topographical data relevant to dispersion of the emissions.

Defining the scope and quantifying the benefits

The air quality guidelines are based on health and ecosystem endpoints determined by consensus. This does not imply that other effects on health and the ecosystem that were not considered in the guidelines may not occur or are unimportant. After assessing the local situation, other health- and ecosystem-related benefit categories should be considered in the analysis.

It is a difficult and comprehensive task to quantify the benefit categories included in a cost–benefit analysis. Some indicators of morbidity, such as the use of medication, the number of hospital admissions or work days lost, can be quantified. Other effects, such as premature death or excess mortality, present more difficult problems. Wellbeing, the quality of life or the value of ecosystems may be very difficult to express in monetary terms. In different countries, values assigned to benefit categories might differ

substantially owing to different cultural attitudes. Despite these uncertainties, it is better to include as many of the relevant benefit categories as possible, even if the economic assessment is uncertain or ambiguous. A clear understanding of the way in which the economic assessment has been undertaken is important and should be reported.

Comparison of benefits with and without control actions

This step involves combining the information on exposure–response relationships with that on air quality assessment, and applying the combined information to the population at risk. Additional data needed in this step include specification of the population at risk, and determination of the prevalence of the different health effects in the population at risk.

Comparison of costs and benefits

Monetary valuation of control actions and of health and environmental effects may be different in concept and vary substantially from country to country. In addition to variations in assessing costs, the relative value of benefit categories, such as benefits to health or building materials, will vary. Thus, the result of comparing costs and benefits in two areas with otherwise similar conditions may differ significantly.

The measures taken to reduce one pollutant may increase or decrease the concentration of other pollutants. These additional effects should be considered, even if they result from exposure to pollutants not under consideration in the primary analysis. Pollutant interactions pose additional complications. Interaction effects may possibly lead to double counting of costs, or to disregarding some costly but necessary action. The same argumentation can be used when estimating benefits.

Sensitivity and uncertainty analysis

Sensitivity analysis includes comparisons of the results of a particular cost–benefit analysis with that of other studies, recalculation of the whole chain of the analysis using other assumptions, or the use of ranges of values. Specifically, a range of values may be used, such as for value of statistical life. Knowledge of the costs of control measures tends to be better developed than that of the benefits to health and ecosystems, and thus costs tend to be more accurately estimated than benefits. In addition, costs tend to be overestimated and benefits underestimated. One important reason for underestimating the benefits is not considering some important benefit categories because of lack of information. Another reason is the variability of the databases available for monetary assessment of benefits.

Many uncertainties are connected with the steps of cost–benefit and cost–effectiveness analysis, such as exposure, exposure–response, control cost estimates and benefits valuation. The results of sensitivity and uncertainty analyses should be presented so as to characterize the impact of major uncertainties on the result of the analysis. In addition, the methods used to conduct the analysis should be clearly described, and the limitations and caveats associated with the analysis should be discussed. Transparency of the analysis is most important.

Involvement of stakeholders and public awareness

The development of standards should encompass a process involving stakeholders that ensures, as much as possible, social equity or fairness to all involved parties. It should also provide sufficient information to guarantee understanding by stakeholders of the scientific and economic consequences. A review by stakeholders of the standard-setting process, initiated at an early stage, is helpful. Transparency in the process of moving from air quality guidelines to standards helps the public to accept necessary measures.

The participation of all those affected by the procedure of standard-setting – industry, local authorities, nongovernmental organizations and the general public – at an early stage of standard derivation is strongly recommended. If these parties are involved in the process at an early stage their cooperation is more likely to be elicited.

Raising public awareness of the health and environmental effects of air pollution is also an important means to obtain public support for necessary control actions, such as with respect to vehicle emissions. Information about the quality of air (such as warnings of air pollution episodes) and the entailed risks (risk communication) should be published in the media to keep the public informed.

IMPLEMENTATION

The main objectives of the implementation of air quality standards are: (*a*) to define the measures needed to achieve the standards; and (*b*) to establish a suitable regulatory strategy and legislative instrument to achieve this goal. Long- as well as medium-term goals are likely to be needed.

The implementation process should ensure a mechanism for regular assessment of air quality, set up the abatement strategies, and establish the enforcement regulations. Also, the impact of control actions should be assessed, both for public health and environmental effects, for example by the

use of epidemiological studies and integrated ecosystems monitoring. Epidemiological studies of the effects of air pollutants on health should be repeated as control measures are implemented. Changes to the mixture of air pollutants and in the composition of complex pollutants such as particulate matter may occur, and changes in exposure–response relationships should be expected.

Assessment of air quality

Air quality assessment has an important role to play within the implementation of an air quality management strategy. The goals of air quality assessment are to provide the air quality management process with relevant data through a proper characterization of the air pollution situation, using monitoring and/or modelling programs and projection of future air quality associated with alternative strategies. Dispersion models can be used very effectively in the design of the definitive monitoring network.

Monitoring methods

The monitoring method (automatic, semi-automatic or manual) adopted for each pollutant should be a standard or reference method, or be validated against such methods. The full description of the method should include information on the sampling and analytical method, on the quality assurance and quality control (internal and external) procedures and on the methods of data management, including data treatment, statistical handling of the data and data validation procedures.

Quality assurance/quality control procedures are an essential part of the measurement system, the aim being to reduce and minimize errors in both the instruments and management of the networks. These procedures should ensure that air quality measurements are consistent (and can be used to give a reliable assessment of ambient air quality) and harmonized over a scale as large as possible, especially in the area of the implementation of the standard.

Design of the monitoring network

An air quality monitoring network can consist of fixed and/or mobile monitoring stations. Although such a network is a fundamental tool for any air quality assessment, its limitations should be borne in mind.

In designing a monitoring network, a primary requirement is to have information about emissions from the dominant and/or most important sources of pollutants. Second, a pilot (or screening) study is needed to gain a good understanding of the geographical distribution of pollutants and to

identify the areas with the highest concentrations. Such a screening study can be performed using dispersion models, with the emission inventory as input, combined with a monitoring study using inexpensive passive samplers in a rather dense network.

The selection strategy for site locations generally varies for different pollutants. The number and distribution of sampling sites required in any network depend on the area to be covered, the spatial variability of the emissions being measured, and the purpose for which the data should be used. Meteorological and topographical conditions as well as the density, type and strength of sources (mobile and stationary) must be considered.

Different types of monitoring station are likely to be needed to provide data at a regional or local level. In monitoring rural and urban areas, specific attention should be paid to sites affected by defined sources such as traffic and other "hot-spots". The representativeness of each site should be defined and assessed. Micro-scale conditions, including the buildings around the stations (street canyons), traffic intensity, the height of the sampling point, distances to obstacles, and the effects of the local sources must be kept in mind.

Air quality modelling

Air quality models are used to establish a relationship between emissions and air quality in a given area, such as a city or region. On the basis of emission data, of atmospheric chemistry, and of meteorological, topographical and geographical parameters, modelling gives an opportunity (*a*) to calculate the projected concentration or deposition of the pollutants in regions, and (*b*) to predict the air pollution level in those areas where air sampling is not performed. Measured concentrations should be used for evaluating and validating models, or even as input data. These measurements improve the accuracy of the concentrations calculated by models by allowing refinement and development of the modelling strategies adopted.

Abatement strategies

Abatement strategies are the set of measures to be taken to reduce pollutant emissions and therefore to improve air quality. Authorities should consider the measures necessary in order to meet the standards. An important factor in selecting abatement strategies is deciding the geographical scale of the area(s) that are considered not to meet the standard(s) and the geographical scale of the area for which control should be applied. In defining the geographical scale for abatement strategies, the extent of the transport of

pollution from neighbouring areas should be considered. This may involve action at supranational, national, regional or local levels.

Supranational, national, regional and local actions form a hierarchy of approaches. Action at the supranational or national level is likely to be most effective in reducing background levels of air pollution. Local air quality management measures may be needed to address specific local problems, and such measures may need to be implemented urgently to deal with special pollution problems. National and supranational plans should specify the extent of the reduction in levels of air pollution that is required and the time-scale for achieving that reduction.

In addition to the comprehensive programme of emission control designed to reduce average pollution levels and the risk of high pollution episodes, short-term actions may be required for the period when the pollution episodes may occur. Such actions, however, should be considered to be applicable in a transitional period only or as a contingency plan. The objective of measures applied on a larger scale is to minimize the occurrence of local air pollution episodes. A link between control of emissions and ambient air quality is required and may need to be demonstrated. Emission-based air quality standards represent one possible step in this process.

Enforcement

The government of each country establishes the responsibilities for implementing air quality standards. Responsibilities for overseeing different aspects of compliance can be distributed among national, regional and local governments depending on the level at which it is necessary to take action.

Success in the enforcement of standards is influenced by the technology applied and the availability of financial resources to industry and government. Compliance with standards may be ensured by various approaches such as administrative penalties or economic incentives. Sufficient staff and other resources are needed to implement the policy actions effectively.

Periodic reports on compliance and trends in pollutant emissions and concentrations should be developed and disseminated to the public. These reports should also predict trends. It is important that the public be aware of the importance of meteorological factors in controlling pollution levels, as these may produce episodes of pollution that are not within the control of the regulatory authorities.

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PART II

EVALUATION OF RISKS TO HUMAN HEALTH

CHAPTER 5

Organic pollutants

5.1 Acrylonitrile

Exposure evaluation

On the basis of large-scale calculations using dispersion models, the average annual ambient air concentration of acrylonitrile in the Netherlands was estimated to be about 0.01 µg/m^3 *(1),* which is below the present detection limit of 0.3 µg/m^3 *(1, 2).* Production figures *(1)* indicate that, in 8 out of 10 European countries for which data are available, ambient concentrations of acrylonitrile are lower or markedly lower than this. Near industrial sites, air concentrations can exceed 100 µg/m^3 over a 24 hour period, but are usually less than 10 µg/m^3 at a distance of about 1 km. Acrylonitrile concentrations in the air at the workplace have exceeded 100 mg/m^3, but shift averages are usually in the range of 1–10 mg/m^3. Exposure from smoking is possible if acrylonitrile is used for tobacco fumigation, and could amount to 20–40 µg daily for an average smoker.

A more sensitive method of determination, with a detection limit below 0.1 µg/m^3, is required in order to examine concentrations in the ambient air and to allow populations at possible risk to be identified.

Health risk evaluation

Acute and noncancer chronic toxicity may occur at concentrations still reported in some industries. Subjective complaints were reported in acute exposure to 35 mg/m^3, and in chronic exposure to 11 mg/m^3, 4.2–7.2 mg/m^3 or 0.6–6 mg/m^3. Teratogenic effects in animals were observed at 174 mg/m^3 and carcinogenicity was shown in rats exposed for 2 years to 44 mg/m^3.

Twelve epidemiological studies investigating the relationship between acrylonitrile exposure and cancer are available; only five indicate a carcinogenic risk from exposure to acrylonitrile *(1).* Negative studies suffered from small cohort size, insufficient characterization of exposure, short follow-up times and relatively young cohorts. Although four of the remaining five epidemiological studies indicate a higher risk of lung cancer, and one study showed a higher mortality rate for liver, gall bladder and cystic duct cancer, all have problems with regard to methodology, definition and/or size of the population, existence of exposure to other carcinogens, and duration of the follow-up period.

In laboratory animals an increased incidence of tumours of the central nervous system, Zymbal gland, stomach, tongue, small intestine and

mammary glands was observed at all doses tested *(3)*. There is nevertheless a clear difference between animal and human studies concerning the tumorigenic response to acrylonitrile: no lung tumours have been produced in animals and no brain tumours have been observed in humans.

Acrylonitrile was placed in IARC Group 2A *(3)* on the basis of sufficient evidence of its carcinogenicity in experimental animals and limited evidence of its carcinogenicity in humans.

The epidemiological study by O'Berg *(4)* presents the clearest available evidence of acrylonitrile as a human lung carcinogen. Furthermore, in this study there were no confounding exposures to other carcinogenic chemicals during exposure to acrylonitrile. It was therefore used to make an estimate of the incremental unit risk. As this study has now been updated to the end of 1983 for cancer incidence and to the end of 1981 for overall mortality, the most recent data are used here *(5)*. Of 1345 workers exposed to acrylonitrile, a total of 43 cases of cancer occurred versus 37.1 expected. Ten cases of lung cancer were observed versus 7.2 expected, based on the company rates. Lung cancer, which had been the focus of the previous report *(4)*, remained in excess but not as high as before; 2 new cases occurred after 1976, with 2.8 expected. This means that the relative risk (RR) would be 10/7.2 = 1.4, significantly lower than in the previous report. On the assumption made by the US Environmental Protection Agency *(6)* for the first O'Berg study *(4)* that the 8-hour time-weighted average exposure was 33 mg/m^3 (15 ppm), and with an estimated work duration of 9 years, the average lifetime daily exposure (X) is estimated to be 930 µg/m^3 (X = 33 mg/m^3 × 8/24 × 240/365 × 9/70).

Using the average relative risk model, the lifetime unit risk (UR) for exposure to 1 µg/m^3 can be calculated to be 1.7×10^{-5} [$UR = P_o(RR - 1)/X = 0.04(1.4 - 1)/930$].

Using animal data, an upper-bound risk of cancer associated with a lifetime inhalation exposure to acrylonitrile was calculated from a rat inhalation study *(7)* to be 1.5×10^{-5} *(6)*.

The calculated unit risk based on the human study is consistent with that of the animal study, although the human estimate is uncertain, particularly because of the lack of documentation on exposure.

Guidelines

Because acrylonitrile is carcinogenic in animals and there is limited evidence of its carcinogenicity in humans, it is treated as if it were a human

carcinogen. No safe level can therefore be recommended. At an air concentration of 1 $\mu g/m^3$, the lifetime risk is estimated to be 2×10^{-5}.

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5.2 Benzene

Exposure evaluation

Sources of benzene in ambient air include cigarette smoke, combustion and evaporation of benzene-containing petrol (up to 5% benzene), petrochemical industries, and combustion processes.

Mean ambient air concentrations of benzene in rural and urban areas are about 1 μg/m^3 and 5–20 μg/m^3, respectively. Indoor and outdoor air levels are higher near such sources of benzene emission as filling stations.

Inhalation is the dominant pathway for benzene exposure in humans. Smoking is a large source of personal exposure, while high short-term exposures can occur during refuelling of motor vehicles. Extended travel in motor vehicles with elevated air benzene levels (from combustion and evaporative emissions) produces exposures reported from various countries that are second only to smoking as contributors to the intensity of overall exposure. The contribution of this source to cumulative ambient benzene exposure and associated cancer risk comprises about 30% when the travel time is one hour, a duration not untypical for urban and suburban commuting by the general population.

Health risk evaluation

The most significant adverse effects from prolonged exposure to benzene are haematotoxicity, genotoxicity and carcinogenicity.

Chronic benzene exposure can result in bone marrow depression expressed as leukopenia, anaemia and/or thrombocytopenia, leading to pancytopenia and aplastic anaemia. Decreases in haematological cell counts and in bone marrow cellularity have been demonstrated in mice after inhalation of concentrations as low as 32 mg/m^3 for 25 weeks. Rats are less sensitive than mice. In humans, haematological effects of varying severity have occurred in workers occupationally exposed to high levels of benzene. Decreased red and white blood cell counts have been reported above median levels of approximately 120 mg/m^3, but not at 0.03–4.5 mg/m^3. Below 32 mg/m^3, there is only weak evidence of effects.

The genotoxicity of benzene has been extensively studied. Benzene does not induce gene mutations in *in vitro* systems, but several studies have

demonstrated induction of both numerical and structural chromosomal aberrations, sister chromatid exchanges and micronuclei in experimental animals and humans after *in vivo* benzene exposure. Some studies in humans have demonstrated chromosomal effects at mean workplace exposures as low as 4–7 mg/m^3. The *in vivo* data indicate that benzene is mutagenic.

The carcinogenicity of benzene has been established both in humans and in laboratory animals. An increased mortality from leukaemia has been demonstrated in workers occupationally exposed. Several types of tumour, primarily of epithelial origin, have been induced in mice and rats after oral exposure and inhalation exposure at 320–960 mg/m^3; these include tumours in the Zymbal gland, liver, mammary gland and nasal cavity. Lymphomas/leukaemias have also been observed, but with lower frequency. The results indicate that benzene is a multisite carcinogen.

Because benzene is characterized as a genotoxic carcinogen and recent data gathered in humans and mice suggest mutagenic potential *in vivo*, establishment of exposure duration and concentration in the human exposure studies is of major importance for the calculation of cancer risk estimates. The Pliofilm cohort is the most thoroughly studied. It was noted that significant exposures to other substances at the studied facilities were probably not a complicating factor, but that exposure estimates for this cohort vary considerably. Three different exposure matrices have been used to describe the Pliofilm cohort, i.e. those reported by Crump & Allen *(1)*, by Rinsky et al. *(2)*, and a newer and more extensive one by Paustenbach et al. *(3)*. The main difference between the first two is that the exposure estimates by Crump & Allen are greater for the early years, during the 1940s. Paustenbach et al. have, among other things, considered short-term, high-level exposure, background concentrations and absorption through the skin, which leads to exposure levels 3–5 times higher than those calculated by Rinsky et al. Compared to the Crump & Allen estimates, Paustenbach et al. arrived at higher exposure estimates for some job classifications, and lower ones for some others.

Within the most recently updated Pliofilm cohort, Paxton et al. *(4, 5)* conducted an extended regression analysis with exposure description for the 15 leukaemia cases and 650 controls. They used all three exposure matrices, which gave estimates of 0.26–1.3 excess cancer cases among 1000 workers at a benzene exposure of 3.2 mg/m^3 (1 ppm) for 40 years (Table 8).

Crump *(7)* calculated unit risk estimates for benzene using the most recently updated data for the Pliofilm cohort and a variety of models

Table 8. Published leukaemia risk estimates for the Plioform cohort at two benzene exposure levels

Cases per 1000 workers exposed to:			
3.2 mg/m³ (1 ppm)	**0.32 mg/m³ (0.1 ppm)**	**Exposure matrix**	**Reference**
5.3	–	Rinsky et al. *(2)*	Brett et al. *(6)*
0.5–1.6	–	Rinsky et al. *(2)*	
		Crump & Allen *(1)*	Brett et al. *(6)*
1.3	0.12	Rinsky et al. *(2)*	Paxton et al. *(4, 5)*
0.26	0.026	Crump & Allen *(1)*	Paxton et al. *(4, 5)*
0.49	0.048	Paustenbach et al. *(3)*	Paxton et al. *(4, 5)*

(Table 9). Multiplicative risk models were found to describe the cohort data better than additive risk models and cumulative exposure better than weighted exposures. Dose–responses were essentially linear when the Crump & Allen exposure matrix was used but, according to the author, there was evidence of concentration-dependent nonlinearity in dose–responses derived using the Paustenbach et al. exposure matrix. In that case, the best-fitting model was quadratic.

As can be seen in Table 9, the concentration-dependent model gives a much lower risk estimate than the other models when the Paustenbach et al. exposure matrix is used. In such a model, the concentration of benzene is raised to the second power and thus given greater weight than the duration of exposure. Although there are biological arguments to support the use of a concentration-dependent model, many of the essential data are preliminary and need to be further developed and peer reviewed.

Models giving equal weight to concentration and duration of exposure have been preferred here for the derivation of a risk estimate. Using multiplicative risk estimates and a cumulative exposure model, Crump *(7)* calculated a unit risk for lifetime exposure of $1.4–1.5 \times 10^{-5}$ per ppb with the Paustenbach et al. exposure matrix, and of 2.4×10^{-5} per ppb with the Crump & Allen exposure matrix. If expressed in µg/m³, the unit risk would thus range from 4.4×10^{-6} to 7.5×10^{-6}. With an additive model instead of a multiplicative model, the risk estimate would have been somewhat smaller. If similar linear extrapolations were done on the occupational cancer risk

Table 9. Model-dependent worker risk and lifetime unit risk estimates for exposure to benzene for the Plioform cohort by Crump *(7)*[a]

Risk estimate	Linear	Nonlinear	Intensity dependent	Exposure reference
Cases per	5.1	5.0	5.1	Crump & Allen *(1)*
1000 workers exposed to 3.2 mg/m^3 (1 ppm)	3.8	2.9	0.036	Paustenbach et al. *(3)*
Unit risk per ppb	2.4×10^{-5}	2.4×10^{-5}	2.4×10^{-5}	Crump & Allen *(1)*
	1.5×10^{-5}	1.4×10^{-5}	1.7×10^{-10}	Paustenbach et al. *(3)*
Unit risk per µg/m^3 [b]	7.5×10^{-6}	7.5×10^{-6}	7.5×10^{-6}	Crump & Allen *(1)*
	4.7×10^{-6}	4.4×10^{-6}	5.3×10^{-11}	Paustenbach et al. *(3)*

[a] Multiplicative risk model, cumulative exposure.

[b] Calculated by converting ppb to µg/m^3.

estimates by Paxton et al. (Table 8), unit risks lower by up to about one order of magnitude would result.

Guidelines

Benzene is carcinogenic to humans and no safe level of exposure can be recommended. For purposes of guideline derivation, it was decided to use the 1994 risk calculation of Crump rather than to derive new estimates. It was recognized that this use of existing analyses of the most recently updated cohort ruled out the inclusion of certain of the analyses noted earlier.

The geometric mean of the range of estimates of the excess lifetime risk of leukaemia at an air concentration of 1 µg/m^3 is 6×10^{-6}. The concentrations of airborne benzene associated with an excess lifetime risk of 1/10 000, 1/100 000 and 1/1 000 000 are, respectively, 17, 1.7 and 0.17 µg/m^3.

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5.3 Butadiene

Exposure evaluation

In a survey of butadiene monomer, polymer and end-user industries in the United States, the geometric mean concentration for full-shift exposure for all job categories was 0.098 ppm and the arithmetic mean was 2.12 ppm *(1)*.

Although data for ambient air levels in Europe are limited, reported concentrations in urban air generally ranged from less than 2 μg/m^3 to 20 μg/m^3 *(2, 3)*. Mean levels in indoor air in a small number of Canadian homes and offices were 0.3 μg/m^3 *(4)*. Sidestream cigarette smoke contains 1,3-butadiene at approximately 0.4 mg/cigarette, and levels of butadiene in smoky indoor environments are typically 10–20 μg/m^3 *(5)*.

Health risk evaluation

Irritation or effects on the central nervous system may be associated with acute exposure to high concentrations of butadiene. Nevertheless, carcinogenicity is considered to be the critical effect for the derivation of air quality guidelines.

1,3-Butadiene has induced a wide variety of tumours in rats and mice, with mice being considerably more sensitive than rats. There are widely divergent points of view as to which animal species – the rat or the mouse – is most appropriate for use in human risk assessments for butadiene *(6, 7)*.

Epidemiological studies, while relatively few in number, suggest that there is equivocal evidence for an association between exposure to butadiene and lymphohaematopoietic cancer. In 1992, IARC classified butadiene in Group 2A (probably carcinogenic to humans). Preliminary (unpublished) reports suggest, however, that there may be an association between butadiene exposure and leukaemia in workers in the synthetic rubber industry.

The genotoxicity of butadiene has been studied in a variety of *in vitro* and *in vivo* mutagenicity assays, and the data overwhelmingly suggest that the induction of cancer requires the metabolism of butadiene to its DNA-reactive metabolites. Butadiene is mutagenic in both bacterial and mammalian systems. The butadiene metabolites epoxybutene and diepoxybutane are also carcinogenic and genotoxic *in vivo*. Butadiene is metabolized to epoxides to a significantly lesser extent in human tissues than in mice and rats. The

differences between mice and rats observed *in vitro* are supported by *in vivo* studies, indicating that mice form very high levels of epoxides compared to rats when exposed to butadiene. In general, the data support the conclusion that the metabolism of butadiene in humans is more similar to that in rats, a relatively insensitive species to butadiene carcinogenicity, than to that in mice, a highly sensitive species. It should be recognized, however, that inter-individual differences in butadiene metabolism may exist that will influence the extent to which butadiene epoxides are formed.

In the only published human study, of 40 individuals occupationally exposed to butadiene at levels typical of an industrial setting (1–3 ppm), there were no significant increases in chromosome aberrations, micronucleus formation or sister chromatid exchanges in peripheral blood lymphocytes *(8)* compared to controls (30 individuals). This observation is of particular interest since butadiene concentrations as low as 6.25 ppm increased the occurrence of the same indicators of genetic damage in the bone marrow and peripheral blood lymphocytes of mice.

Several different risk assessments have been conducted for butadiene, and a number of these for occupational exposures to butadiene have been summarized by the US Occupational Safety and Health Administration *(9)*. The estimates in these risk assessments were based on different assumptions. Some were adjusted for absorbed dose, since changes in butadiene absorption will occur in animals with changes in the inhaled concentration *(10)*. For the most part, they were based on the multistage model. There was considerable variation in human cancer risk estimates depending on the animal species used for the calculations, with those based on tumour data in mice being 100–1000 times higher than those based on tumour data in rats.

Unit risk estimates for cancer associated with continuous lifetime exposure to butadiene in ambient air have been reported *(11–13)*. Values estimated by the Californian Air Resources Board in 1992 *(11)*, based on adjustment of dose for absorption *(10)* and tumour incidence in mice *(14)* and rats *(15)*, were 0.0098 and 0.8 per ppm, respectively. The value estimated by the US Environmental Protection Agency's Integrated Risk Information System (IRIS), based on linearized multistage modelling of data from an earlier, limited US National Toxicology Program (NTP) bioassay in mice, was 2.8×10^{-4} per $\mu g/m^3$ *(12)*. Values estimated by the National Institute of Public Health and Environmental Protection (RIVM) in the Netherlands, based on linearized multistage modelling of the incidence of lymphocytic lymphoma and haemangiosarcomas of the heart in mice in the most recent NTP bioassay *(14)*, were in the range $0.7–1.7 \times 10^{-5}$ per $\mu g/m^3$ *(13)*.

Estimates of human cancer risk could be improved by the inclusion of mechanistic information such as *in vivo* toxicokinetic data, genotoxicity data, and data from the recent epidemiology reassessment. For example, new data on levels of butadiene epoxides in blood and tissues in laboratory animals *(16–18)* could be used to replace the earlier absorption data *(10)*. Additionally, physiologically based pharmacokinetic models developed since earlier attempts to apply this approach to risk assessment have been greatly improved, most notably by the incorporation of model parameters that have been experimentally measured rather than empirically estimated. None the less, none of the models published to date incorporates the necessary information on the formation, removal and distribution of diepoxybutane.

Guidelines

Quantitative cancer risk estimates vary widely, in particular depending on the test species used. No definitive conclusions can yet be made as to which species should be used for risk estimates. New, as yet unpublished epidemiological data might have an impact on the risk estimates and hence on the derivation of a guideline value. In the light of these considerations, no guideline value can be recommended at this time.

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5.4 Carbon disulfide

Exposure evaluation

Inhalation represents the main route of entry of carbon disulfide into the human organism. Values in the vicinity of viscose rayon plants range from 0.01 mg/m^3 to about 1.5 mg/m^3, depending mostly on the distance from the source.

Health risk evaluation

A summary of the most relevant concentration–response findings is given in Table 10.

In the light of numerous epidemiological studies, it is very difficult to establish the exact exposure–time relationship. During the approximate period 1955–1965, carbon disulfide concentrations in viscose rayon plants averaged about 250 mg/m^3; they were subsequently reduced to 50–150 mg/m^3 and more recently to 20–30 mg/m^3. It is thus practically impossible to evaluate the long-term (five or more years) exposure level in a retrospective study. Moreover, most exposure data in occupational studies are not reliable, owing to poor measurement methodology. It is necessary to keep this in mind also when studying Table 10.

At exposure levels of 30 mg/m^3 and above, observable adverse health effects have been well established. The coronary heart disease rate increases at levels of 30–120 mg/m^3 of carbon disulfide after an exposure of more than 10 years. Effects on the central and peripheral nervous systems and the vascular system have been established in the same range of concentrations after long-term exposure. Functional changes of the central nervous system have even been observed at lower concentrations (20–25 mg/m^3).

Some authors claim to have observed adverse health effects in workers exposed to 10 mg/m^3 of carbon disulfide for 10–15 years. Because of the lack of reliable retrospective data on exposure levels, however, the dose–response relationship governing these findings is difficult to establish.

Guidelines

The lowest concentration of carbon disulfide at which an adverse effect was observed in occupational exposure was about 10 mg/m^3, which may be equivalent to a concentration in the general environment of 1 mg/m^3. In

Table 10. Some concentration–response relationships in occupational exposure to carbon disulfide

Carbon disulfide concentration (mg/m^3)	Duration of exposure (years)	Symptoms and signs	Reference
500–2500	0.5	Polyneuritis, myopathy, acute psychosis	*1*
450–1000	< 0.5	Polyneuritis, encephalopathy	*2*
200–500	1–9	Increased ophthalmic pressure	*3*
60–175	5	Eye burning, abnormal pupillary light reactions	*4*
31–137	10	Psychomotor and psychological disturbances	*5*
29–118	15	Polyneuropathy, abnormal EEG, conduction velocity slowed, psychological changes	*6, 7*
29–118	10	Increase in coronary mortality, angina pectoris, slightly higher systolic and diastolic blood pressure	*8–11*
40–80	2	Asthenospermia, hypospermia, teratospermia	*12*
22–44	> 10	Arteriosclerotic changes and hypertension	*13*
30–50	> 10	Decreased immunological reactions	*14*
30	3	Increase in spontaneous abortions and premature births	*15*
20–25	< 5	Functional disturbances of the central nervous system	*16, 17*
10	10–15	Sensory polyneuritis, increased pain threshold	*18*
10	10–15	Depressed blood progesterone, increased estriol, irregular menstruation	*19*

selecting the size of the protection (safety) factor, the expected variability in the susceptibility of the general population was taken into account, and a protection factor of 10 was considered appropriate. This leads to the recommendation of a guideline value of 100 μg/m^3, with an averaging time of 24 hours. It is believed that below this value adverse health effects of environmental exposure to carbon disulfide (outdoor or indoor) are not likely to occur.

If carbon disulfide is used as the index substance for viscose emissions, odour perception is not to be expected when carbon disulfide peak concentration is kept below one tenth of its odour threshold value, i.e. below 20 μg/m^3. Based on the sensory effects of carbon disulfide, a guideline value of 20 μg/m^3 (average time 30 minutes) is recommended.

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5.5 Carbon monoxide

Exposure evaluation

Global background concentrations of carbon monoxide range between 0.06 mg/m^3 and 0.14 mg/m^3 (0.05–0.12 ppm). In urban traffic environments of large European cities, the 8-hour average carbon monoxide concentrations are generally lower than 20 mg/m^3 (17 ppm) with short-lasting peaks below 60 mg/m^3 (53 ppm). Carbon monoxide concentrations inside vehicles are generally higher than those measured in ambient outdoor air. The air quality data from fixed-site monitoring stations seem to reflect rather poorly short-term exposures of various urban population groups, but appear to reflect better longer averaging times, such as 8 hours.

In underground and multistorey car parks, road tunnels, enclosed ice arenas and various other indoor microenvironments, in which combustion engines are used under conditions of insufficient ventilation, the mean levels of carbon monoxide can rise above 115 mg/m^3 (100 ppm) for several hours, with short-lasting peak values that can be much higher. In homes with gas appliances, peak carbon monoxide concentrations of up to 60–115 mg/m^3 (53–100 ppm) have been measured. Environmental tobacco smoke in dwellings, offices, vehicles and restaurants can raise the 8-hour average carbon monoxide concentration to 23–46 mg/m^3 (20–40 ppm).

Carbon monoxide diffuses rapidly across alveolar, capillary and placental membranes. Approximately 80–90% of the absorbed carbon monoxide binds with haemoglobin to form carboxyhaemoglobin (COHb), which is a specific biomarker of exposure in blood. The affinity of haemoglobin for carbon monoxide is 200–250 times that for oxygen. During an exposure to a fixed concentration of carbon monoxide, the COHb concentration increases rapidly at the onset of exposure, starts to level off after 3 hours, and reaches a steady state after 6–8 hours of exposure. The elimination half-life in the fetus is much longer than in the pregnant mother.

In real-life situations, the prediction of individual COHb levels is difficult because of large spatial and temporal variations in both indoor and outdoor carbon monoxide concentrations.

Health risk evaluation

The binding of carbon monoxide with haemoglobin to form COHb reduces the oxygen-carrying capacity of the blood and impairs the release of

oxygen from haemoglobin to extravascular tissues. These are the main causes of tissue hypoxia produced by carbon monoxide at low exposure levels. At higher concentrations the rest of the absorbed carbon monoxide binds with other haem proteins such as myoglobin, and with cytochrome oxidase and cytochrome P-450 *(1, 2)*. The toxic effects of carbon monoxide become evident in organs and tissues with high oxygen consumption such as the brain, the heart, exercising skeletal muscle and the developing fetus.

Severe hypoxia due to acute carbon monoxide poisoning may cause both reversible, short-lasting neurological deficits and severe, often delayed neurological damage. The neurobehavioural effects include impaired coordination, tracking, driving ability, vigilance and cognitive performance at COHb levels as low as 5.1–8.2% *(3–5)*.

In apparently healthy subjects, maximal exercise performance has decreased at COHb levels as low as 5%. The regression between the percentage decrease in maximal oxygen consumption and the percentage increase in COHb concentration appears to be linear, with a fall in oxygen consumption of approximately one percentage point for each percentage point rise in COHb level above 4% *(1, 6)*.

In controlled human studies involving patients with documented coronary artery disease, mean postexposure COHb levels of 2.9–5.9% (corresponding to postexercise COHb levels of 2.0–5.2%) have been associated with a significant shortening in the time to onset of angina, with increased electrocardiographic changes and with impaired left ventricular function during exercise *(7–11)*. In addition, ventricular arrhythmias may be increased significantly at the higher range of mean postexercise COHb levels *(12, 13)*. Epidemiological and clinical data indicate that carbon monoxide from recent smoking and environmental or occupational exposures may contribute to cardiovascular mortality and the early course of myocardial infarction *(1)*. According to one study there has been a 35% excess risk of death from arteriosclerotic heart disease among smoking and nonsmoking tunnel officers, in whom the long-term mean COHb levels were generally less than 5% *(13)*. Current data from epidemiological studies and experimental animal studies indicate that common environmental exposures to carbon monoxide do not have atherogenic effects on humans *(1, 14)*.

During pregnancy, endogenous production of carbon monoxide is increased so that maternal COHb levels are usually about 20% higher

than the non-pregnant values. At steady state, fetal COHb levels are up to 10–15% higher than maternal COHb levels *(1, 15)*. There is a well established and probably causal relationship between maternal smoking and low birth weight at fetal COHb levels of 2–10%. In addition, maternal smoking seems to be associated with a dose-dependent increase in perinatal deaths and with behavioural effects in infants and young children *(15)*.

In contrast with most other man-made air pollutants at very high concentrations (well above ambient levels), carbon monoxide causes a large number of acute accidental and suicidal deaths in the general population.

Guidelines

In healthy subjects, endogenous production of carbon monoxide results in COHb levels of 0.4–0.7%. During pregnancy, elevated maternal COHb levels of 0.7–2.5%, mainly due to increased endogenous production, have been reported. The COHb levels in non-smoking general populations are usually 0.5–1.5%, owing to endogenous production and environmental exposures. Nonsmokers in certain occupations (car drivers, policemen, traffic wardens, garage and tunnel workers, firemen, etc.) can have long-term COHb levels of up to 5%, and heavy cigarette smokers have COHb levels of up to 10% *(1, 2, 15)*. Well trained subjects engaging in heavy exercise in polluted indoor environments can increase their COHb levels quickly up to 10–20%. In indoor ice arenas, epidemic carbon monoxide poisonings have recently been reported.

To protect nonsmoking, middle-aged and elderly population groups with documented or latent coronary artery disease from acute ischaemic heart attacks, and to protect the fetuses of nonsmoking pregnant women from untoward hypoxic effects, a COHb level of 2.5% should not be exceeded.

The following guidelines are based on the Coburn-Foster-Kane exponential equation, which takes into account all the known physiological variables affecting carbon monoxide uptake *(16)*. The following guideline values (ppm values rounded) and periods of time-weighted average exposures have been determined in such a way that the COHb level of 2.5% is not exceeded, even when a normal subject engages in light or moderate exercise:

- 100 mg/m^3 (90 ppm) for 15 minutes
- 60 mg/m^3 (50 ppm) for 30 minutes
- 30 mg/m^3 (25 ppm) for 1 hour
- 10 mg/m^3 (10 ppm) for 8 hours

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5.6 1,2-Dichloroethane

Exposure evaluation

Rural or background atmospheric concentrations in western Europe and North America are approximately 0.2 μg/m^3, and the limited data available on indoor concentrations show that they are about the same. Average levels in cities vary from 0.4 μg/m^3 to 1.0 μg/m^3, increasing to 6.l μg/m^3 near petrol stations, parking garages and production facilities.

Health risk evaluation

Human studies point to effects on the central nervous system and the liver, but the limited data do not allow a definitive conclusion regarding a LOAEL or NOAEL. In animals, long-term inhalation exposure (> 6 months) to 1,2-dichloroethane levels of approximately 700 mg/m^3 and above has been shown to result in histological changes in the liver *(1–3).* The same animal studies reported no adverse histological changes in the liver and kidneys of guinea pigs and rats at levels of about 400 mg/m^3. Findings concerning effects on reproduction are contradictory.

Animal data suggest a NOAEL in laboratory animals of 400 mg/m^3 and a LOAEL of 700 mg/m^3.

With regard to mutagenicity as an endpoint and to the causal connections between DNA damage and the initiation of carcinogenicity, 1,2-dichloroethane has been shown to be weakly mutagenic in *Salmonella typhimurium,* both in the absence and in the presence of microsomal activation systems. It has also been demonstrated to be mutagenic in other test species and in *in vitro* tests using mammalian cells.

In a lifetime study in rats and mice in which 1,2-dichloroethane was administered by gavage, it caused tumours at multiple sites in both species. In the only inhalation study performed *(4),* exposure to 1,2-dichloroethane did not result in an increased tumour incidence. The negative results obtained in this study, however, do not detract from the positive findings of the oral study *(5, 6)* when differences in total dose, exposure time and pharmacokinetics are considered.

1,2-Dichloroethane was evaluated in 1979 by IARC as a chemical for which there is sufficient evidence of carcinogenicity in experimental animals and inadequate evidence in humans *(7).* To date there are two publications

giving quantitative carcinogenic risk estimates based on animal data. One, developed by the National Institute of Public Health in the Netherlands on the basis of oral exposure of rats by gavage *(6),* indicates a lifetime risk of one in a million from exposure to 0.48 μg/m^3 *(8),* which corresponds to a unit risk of about 2×10^{-6}. The US Environmental Protection Agency *(9)* has estimated an incremental unit risk of 2.6×10^{-5} on the basis of data from gavage studies and of 1×10^{-6} on the basis of a negative inhalation study.

Guidelines

Evidence of carcinogenicity in animals is sufficient on the basis of oral ingestion data. However, animal inhalation data do not at present provide positive evidence. Because of deficiencies in extrapolation from oral data to inhalation, the two risk estimates available are not used in the guidelines.

For noncarcinogenic endpoints, data from animal studies imply a NOAEL of about 400 mg/m^3 and suggest a LOAEL of about 700 mg/m^3. A protection (safety) factor of 1000 is considered appropriate in extrapolation of animal data to the general population. In selecting such a large protection factor, variations in exposure time, the limitations of the database and the fact that a no-effect level in humans cannot be established are of decisive importance. The resulting value of 0.7 mg/m^3 for continuous exposure (averaging time 24 hours) is recommended as a guideline value. Since this value is above current environmental levels and present exposures are not of concern to health, this guideline relates only to accidental release episodes or specific indoor pollution problems.

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5.7 Dichloromethane

Exposure evaluation

Mean outdoor concentrations of dichloromethane are generally below 5 μg/m^3 *(1–4)*. Significantly higher concentrations (by at least one order of magnitude) may occur close to industrial emission sources. Indoor air concentrations are variable but tend to be about three times greater than outdoor values *(5, 6)*. Under certain circumstances, much higher values (up to 4000 μg/m^3) may be recorded indoors, particularly with use of paint stripping solutions *(7)*. Exposures of the general population occur principally through the use of dichloromethane-containing consumer products. Exposure in outdoor air, water *(8–12)* and food *(13–15)* is low.

Health risk evaluation

The critical effects of dichloromethane include effects on the central nervous system, the production of carboxyhaemoglobin (COHb) and carcinogenicity. The impairment of behavioural or sensory responses may occur in humans following acute inhalation exposure at levels exceeding 1050 mg/m^3 (300 ppm) for short durations, and the effects are transient. The cytochrome P-450-related oxidative pathway resulting in carbon monoxide production is saturable, producing maximum blood COHb levels of $\leq$ 9%. Nevertheless, these COHb levels are sufficiently high to induce acute effects on the central nervous system, and it thus appears that such effects are probably due to COHb production. Dichloromethane does not appear to cause serious effects in humans at those relatively high levels reported in occupational settings.

Although there is no convincing evidence of cancer incidence associated with occupational exposure, the available data have limitations and are considered inadequate to assess human carcinogenicity. In male and female mice and male and female rats, the National Toxicology Program's bioassays led to the conclusion of clear evidence of carcinogenicity in mice, clear evidence in female rats and equivocal evidence in male rats *(16)*. IARC has classified dichloromethane as showing sufficient evidence of carcinogenicity in experimental animals (Group 2B) *(17)*.

The health risks of exposure to dichloromethane have been considered in detail by an International Programme on Chemical Safety (IPCS) expert group. Given the data on interspecies differences in metabolism and comparative cancer risks, that group concluded that carcinogenicity was not the

critical endpoint for risk assessment purposes. It is therefore concluded that the formation of COHb is a more direct indication of a toxic effect, that it can be monitored, and that it is therefore more suitable as a basis for the derivation of a guideline. Furthermore, it is unlikely that ambient air exposures represent a health concern with reference to any cancer endpoint, since concentrations of dichloromethane in ambient air are orders of magnitude lower than levels associated with direct adverse effects on the central nervous system or on COHb production in humans.

The application of physiologically based pharmacokinetic models to the available animal data lead to small risk estimates *(18, 19)*. These risk estimates are much lower than the recommended guideline value using COHb formation, and were therefore not employed in guideline derivation.

Guidelines

The selected biological endpoint of interest is the formation of COHb, which is measured in the blood of normal subjects at levels of 0.50–1.5% of total haemoglobin. In heavy smokers, the level of COHb may range up to 10%. Carbon monoxide from various sources may contribute to the formation of COHb. Since overall levels in many cases approach the recommended maximum of 3%, it is prudent to minimize any additional amounts of COHb contributed from dichloromethane. It was thus concluded that no more than 0.1% additional COHb should be formed from dichloromethane exposure. This corresponds to the analytical reproducibility of the method applied to measure COHb at the level of concern. This maximum allowable increase in COHb corresponds to a 24-hour exposure to dichloromethane at a concentration of 3 mg/m^3. Consequently, a guideline value of 3 mg/m^3 is recommended. In addition, the weekly average concentration should not exceed one seventh (0.45 mg/m^3) of this 24-hour guideline, given the half-life of COHb.

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5.8 Formaldehyde

Exposure evaluation

The major route of exposure to formaldehyde is inhalation. Table 11 shows the contribution of the various atmospheric environments to non-occupational air levels. Indoor air concentrations are several orders of magnitude higher than levels in ambient air. Owing to the extremely high concentrations of formaldehyde in tobacco smoke, smoking constitutes a major source of formaldehyde *(1)*.

Health risk evaluation

Predominant symptoms of formaldehyde exposure in humans are irritation of the eyes, nose and throat, together with concentration-dependent discomfort, lachrymation, sneezing, coughing, nausea, dyspnoea and finally death (Table 12) .

Damage to the nasal mucosa, such as squamous cell metaplasia and mild dysplasia of the respiratory epithelium, have been reported in humans, but

Table 11. Average exposure concentrations to formaldehyde and contribution of various atmospheric environments to average exposure to formaldehyde

Source	Concentration (mg/m^3)	Exposure (mg/day)
Ambient air (10% of time; 2 m^3/day)	0.001–0.02	0.002–0.04
Indoor air		
Home (65% of time; 10 m^3/day)		
– conventional	0.03–0.06	0.3–0.6
– mobile home	0.1	1.0
– environmental tobacco smoke	0.05–0.35	0.5–3.5
Workplace (25% of time; 8 m^3/day)		
– without occupational exposure [a]	0.03–0.06	0.2–0.5
– with occupational exposure	1.0	8.0
– environmental tobacco smoke	0.05–0.35	0.4–2.8
Smoking (20 cigarettes/day)	60–130	0.9–2.0 [b]

[a] Assuming the normal formaldehyde concentration in conventional buildings.

[b] Total amount of formaldehyde in smoke from 20 cigarettes.

Source: World Health Organization *(2)*.

Table 12. Effects of formaldehyde in humans after short-term exposure

Concentration range or average (mg/m³)	Time range or average	Health effects in general population
0.03	Repeated exposure	Odour detection threshold (10th percentile) [a]
0.18	Repeated exposure	Odour detection threshold (50th percentile) [a]
0.6	Repeated exposure	Odour detection threshold (90th percentile) [a]
0.1–3.1	Single and repeated exposure	Throat and nose irritation threshold
0.6–1.2	Single and repeated exposure	Eye irritation threshold
0.5–2.0	3–5 hours	Decreased nasal mucus flow rate
2.4	40 minutes on 2 successive days with 10 minutes of moderate exercise on second day	Postexposure (up to 24 hours) headache
2.5–3.7	–[b]	Biting sensation in eyes and nose
3.7	Single and repeated exposure	Decreased pulmonary function only at heavy exercise
5–6.2	30 minutes	Tolerable for 30 minutes with lachrymation
12–25	–[b]	Strong lachrymation, lasting for 1 hour
37–60	–[b]	Pulmonary oedema, pneumonia, danger to life
60–125	–[b]	Death

[a] Frequency of effect in population.

[b] Time range or average unspecified.

these findings may have been confounded by concomitant exposures to other substances *(3)*.

There is convincing evidence of high concentrations of formaldehyde being capable of inducing nasal cancer in rats and possibly in mice *(3)*. Formaldehyde has been shown to be genotoxic in a variety of *in vitro* and *in vivo*

systems *(3)*. There is also epidemiological evidence of associations between relatively high occupational exposure to formaldehyde and both nasopharyngeal and sinonasal cancers *(3–7)*.

There is substantial variation in individual responses to formaldehyde in humans *(1–3)*. Significant increases in signs of irritation occur at levels above 0.1 mg/m^3 in healthy subjects. At concentrations above 1.2 mg/m^3, a progression of symptoms and effects occurs. Lung function of healthy nonsmokers and asthmatics exposed to formaldehyde at levels up to 3.7 mg/m^3 was generally unaltered *(8–10)*. It is assumed that in these studies the observed effects were more related to peak concentrations than to mean values.

There is some evidence of formaldehyde inducing pathological and cytogenetic changes in the nasal mucosa of humans. Reported mean exposures ranged from 0.02 mg/m^3 to 2.4 mg/m^3, with peaks between 5 mg/m^3 and 18 mg/m^3. Epidemiological studies suggest a causal relationship between exposure to formaldehyde and nasopharyngeal cancer, although the conclusion is tempered by the small numbers of observed and expected cases *(3–6)*. There are also epidemiological observations of an association between relatively high occupational exposures to formaldehyde and sinonasal cancer *(7)*. IARC *(3)* has interpreted the available cancer data as limited evidence for the carcinogenicity of formaldehyde in humans, and classified formaldehyde in Group 2A.

Formaldehyde is a nasal carcinogen in rats. A highly significant incidence of nasal cancer was found in rats exposed to a level of 16.7 mg/m^3, but the dose–response curve was nonlinear, the risk being disproportionately low at low concentrations. It also appears that the dose–response curves were nearly identical for neoplastic changes, cell turnover, DNA–protein cross-links and hyperproliferation, when the relationship between non-neoplastic and neoplastic lesions in the nasal respiratory epithelium was analysed. This close concordance indicates an association among the observed cytotoxic, genotoxic and carcinogenic effects. It is thus likely that hyperproliferation induced by cytotoxicity plays a significant role in the formation of nasal tumours by formaldehyde.

Despite differences in the anatomy and physiology of the respiratory tract between rats and humans, the respiratory tract defence mechanisms are similar. It is therefore reasonable to assume that the response of the human respiratory tract mucosa to formaldehyde will be similar to that of the rat. Thus, if the respiratory tract tissue is not repeatedly damaged, exposure of

humans to low, noncytotoxic concentrations of formaldehyde can be assumed to be associated with a negligible cancer risk. This is consistent with epidemiological findings of excess risks of nasopharyngeal and sinonasal cancers associated with concentrations above about 1 mg/m^3.

Simultaneous exposure of humans to formaldehyde and other upper respiratory tract toxicants, such as acrolein, acetaldehyde, crotonaldehyde, furfural, glutaraldehyde and ozone, may lead to additive or synergistic effects, in particular with respect to sensory irritation and possibly also regarding cytotoxic effects on the nasal mucosa *(3, 11–16)*.

Guidelines

The lowest concentration that has been associated with nose and throat irritation in humans after short-term exposure is 0.1 mg/m^3, although some individuals can sense the presence of formaldehyde at lower concentrations.

To prevent significant sensory irritation in the general population, an air quality guideline value of 0.1 mg/m^3 as a 30-minute average is recommended. Since this is over one order of magnitude lower than a presumed threshold for cytotoxic damage to the nasal mucosa, this guideline value represents an exposure level at which there is a negligible risk of upper respiratory tract cancer in humans.

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5.9 Polycyclic aromatic hydrocarbons

Exposure evaluation

Polycyclic aromatic hydrocarbons (PAHs) are formed during incomplete combustion or pyrolysis of organic material and in connection with the worldwide use of oil, gas, coal and wood in energy production. Additional contributions to ambient air levels arise from tobacco smoking, while the use of unvented heating sources can increase PAH concentrations in indoor air. Because of such widespread sources, PAHs are present almost everywhere. PAHs are complex mixtures of hundreds of chemicals, including derivatives of PAHs, such as nitro-PAHs and oxygenated products, and also heterocyclic PAHs. The biological properties of the majority of these compounds are as yet unknown. Benzo[*a*]pyrene (BaP) is the PAH most widely studied, and the abundance of information on toxicity and occurrence of PAHs is related to this compound. Current annual mean concentrations of BaP in major European urban areas are in the range 1–10 ng/m^3. In rural areas, the concentrations are < 1 ng/m^3 *(1–5)*.

Food is considered to be the major source of human PAH exposure, owing to PAH formation during cooking or from atmospheric deposition of PAHs on grains, fruits and vegetables. The relative contribution of airborne PAH pollutants to food levels (via fallout) has not been well characterized *(6)*.

Health risk evaluation

Data from animal studies indicate that several PAHs may induce a number of adverse effects, such as immunotoxicity, genotoxicity, carcinogenicity and reproductive toxicity (affecting both male and female offspring), and may possibly also influence the development of atherosclerosis. The critical endpoint for health risk evaluation is the well documented carcinogenicity of several PAHs *(7)*.

BaP is by far the most intensively studied PAH in experimental animals. It produces tumours of many different tissues, depending on the species tested and the route of application. BaP is the only PAH that has been tested for carcinogenicity following inhalation, and it produced lung tumours in hamsters, the only species tested. Induction of lung tumours in rats and hamsters has also been documented for BaP and several other PAHs following direct application, such as intratracheal instillation into the pulmonary tissue. The lung carcinogenicity of BaP can be enhanced by coexposure to other substances such as cigarette smoke, asbestos and probably also

airborne particles. Several studies have shown that the benzene-soluble fraction, containing 4- to 7-ring PAHs of condensates from car exhausts, domestic coal-stove emissions and tobacco smoke, contains nearly all the carcinogenic potential of PAHs from these sources *(8)*.

Because several PAHs have been shown to be carcinogenic, and many more have been shown to be genotoxic in *in vitro* assays, a suitable indicator for the carcinogenic fraction of the large number of PAHs in ambient air is desirable. The most appropriate indicator for the carcinogenic PAHs in air seems to be BaP concentrations, given present knowledge and the existing database. Assessment of risks to health of a given mixture of PAHs using this indicator approach would entail, first, measurement of the concentration of BaP in a given mixture present in a medium such as air. Then, assuming that the given mixture resembles that from coke ovens, the unit risk estimate is applied in tandem with the measured BaP air concentration to obtain the lifetime cancer risk at this exposure level.

The proportions of different PAHs detected in different emissions and workplaces sometimes differ widely from each other and from PAH profiles in ambient air. Nevertheless, the profiles of PAHs in ambient air do not seem to differ very much from one area to another, although large variations may be seen under special conditions. Furthermore, the carcinogenicity of PAH mixtures may be influenced by synergistic and antagonistic effects of other compounds emitted together with PAHs during incomplete combustion. It should also be recognized that in ambient air the carcinogenic 4- to 7-ring PAHs (representing the majority of PAHs) are preferentially attached to particles and only a minor fraction, depending on the temperature, exists as volatiles. A few studies indicate that the toxicokinetic properties of inhaled BaP attached to particles are different from those of pure BaP alone. Virtually nothing is known about other PAHs in this respect.

Risk assessments and potency assessments of various individual PAHs and complex mixtures of PAHs have been attempted. BaP is the only PAH for which a database is available, allowing a quantitative risk assessment. Risk assessment of BaP is, however, hampered by the poor quality of the data sets available *(9)*.

Attempts to derive relative potencies of individual PAHs (relative to BaP) have also been published, and the idea of summarizing the contributions from each of the selected PAHs into a total BaP equivalent dose (assuming their carcinogenic effects to be additive) has emerged *(10, 11)*. There are doubts, however, about the scientific justification for these procedures.

Risk estimates considered in the United States for coke-oven emissions were used in the first edition of these guidelines. Using a linearized multistage model, the most plausible upper-bound individual lifetime unit risk estimate associated with a continuous exposure to 1 μg/m^3 of benzene-soluble compounds of coke-oven emissions in ambient air was approximately 6.2×10^{-4}. Using BaP as an indicator of general PAH mixtures from emissions of coke ovens and similar combustion processes in urban air, and a reported value of 0.71% BaP in the benzene-soluble fraction of coke oven emissions, a lifetime risk of respiratory cancer of 8.7×10^{-5} per ng/m^3 was calculated *(1)*.

From the lung tumour rates obtained in a recent rat inhalation study with coal tar/pitch condensation aerosols, containing two different levels of BaP, a lifetime tumour risk of 2×10^{-5} per ng/m^3 for BaP as a constituent of a complex mixture was calculated using a linearized multistage model *(12)*.

Guidelines

No specific guideline value can be recommended for PAHs as such in air. These compounds are typically constituents of complex mixtures. Some PAHs are also potent carcinogens, which may interact with a number of other compounds. In addition, PAHs in air are attached to particles, which may also play a role in their carcinogenicity. Although food is thought to be the major source of human exposure to PAHs, part of this contamination may arise from air pollution with PAHs. The levels of PAHs in air should therefore be kept as low as possible.

In view of the difficulties in dealing with guidelines for PAH mixtures, the advantages and disadvantages of using a single indicator carcinogen to represent the carcinogenic potential of a fraction of PAH in air were considered. Evaluation of, for example, BaP alone will probably underestimate the carcinogenic potential of airborne PAH mixtures, since co-occurring substances are also carcinogenic. Nevertheless, the well studied common constituent of PAH mixtures, BaP, was chosen as an indicator, although the limitations and uncertainties in such an approach were recognized.

To set priorities with respect to control, an excess lifetime cancer risk, expressed in terms of the BaP concentration and based on observations in coke-oven workers exposed to mixtures of PAHs, is presented here. It must be emphasized that the composition of PAHs to which coke-oven workers are exposed may not be similar to that in ambient air, although it was noted that similar risks have been derived from studies of individuals exposed to other mixtures containing PAHs. Having also taken into consideration

some recent animal data from which a unit risk of the same order of magnitude can be derived, it was concluded that the occupational epidemiology data should serve as the basis for the risk estimate.

Based on epidemiological data from studies in coke-oven workers, a unit risk for BaP as indicator air constituent for PAHs is estimated to be 8.7×10^{-5} per ng/m^3, which is the same as that established by WHO in 1987. The corresponding concentrations of BaP producing excess lifetime cancer risks of 1/10 000, 1/100 000 and 1/1 000 000 are 1.2, 0.12 and 0.012 ng/m^3, respectively.

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5.10 Polychlorinated biphenyls

Exposure evaluation

Analysis of polychlorinated biphenyls (PCBs) should be performed by congener-specific methods. The method of quantifying total PCBs, by comparing the sample peak pattern with that of a commercial mixture, is accurate only when the sample under investigation has been directly contaminated by a commercial mixture. Because of substantial differences in PCB patterns between biological samples and technical products, however, this method leads to errors in the quantification of biological samples and also to differences between laboratories owing to the use of different standard mixtures. As a consequence, data have to be interpreted with great care. Comparisons can only be made between data either from the same laboratory, using the same validated technique and the same standards over a longer period, or from different laboratories when very strict interlaboratory controls have been applied. Indications of trends can only be obtained when these considerations are taken into account.

Food

Food is the main source of human intake of PCBs; intake through drinking-water is negligible.

The daily intake of total PCBs in Sweden was recently estimated at 0.05 µg/kg body weight (BW), with a 50% contribution from fish *(1)*. This is markedly lower than an earlier Finnish estimate of 0.24 µg/kg BW *(2)*, and might reflect the decreasing trends in PCB levels in Nordic food. Recent data from the Nordic countries indicate that the current average daily intake in toxic equivalents of dioxin-like PCBs may be slightly above 1 pg/kg BW *(3, 4)*.

If the contributions of PCDDs and PCDFs are also taken into account, the daily intake in toxic equivalents would be in the range 2–6 pg/kg BW for many European countries and the United States *(5)*. For certain risk groups, such as fishermen from the Baltic Sea and Inuits in the Arctic who consume large amounts of contaminated fatty fish, the intake may be up to four times higher.

Air

PCB levels have been shown to be higher in indoor air than in ambient air. Inhalation exposure to PCBs, assuming an indoor air level of 3 ng/m^3 in an uncontaminated building and an inhaled volume of 20 m^3 of air per day for

adults, is approximately 0.001 µg/kg BW per day. In contaminated buildings concentrations above 300 ng/m^3 have been found, corresponding to a daily dose of at least 0.1 µg/kg BW. In buildings using PCB-containing sealants, levels up to 7500 ng/m^3 have been found (corresponding to a daily dose of 2.5 µg/kg BW). In ambient air there is a wide variation in the measurements from nonindustrialized (e.g. 0.003 ng/m^3) and industrial/urban areas (e.g. 3 ng/m^3). The levels of dioxin-like PCBs cannot be estimated owing to the lack of congener-specific analytical data.

Health risk evaluation

In 1990, the Joint FAO/WHO Expert Committee on Food Additives concluded that, owing to the limitations of the available data, it was impossible to establish a precise numerical value for a tolerable intake of total PCBs for humans *(6)*. IARC concluded that available studies suggested an association between human cancer and exposure to PCBs *(7)*. Overall, PCBs were classified as probably carcinogenic to humans (Group 2A), although several national governments are employing tolerable daily intakes (TDIs) for PCBs for the purpose of risk management.

In Germany a TDI for PCB of 1–3 µg/kg BW has been suggested. It was also recommended that, for precautionary reasons, the proportional daily intake via indoor air should not exceed 10% of the TDI for long periods. On this basis an action level for source removal of 3000 µg/m^3 has been derived. For concentrations between 3000 ng/m^3 and 10 000 ng/m^3 (that is, between 3 µg/m^3 and 10 µg/m^3) a concrete health risk is not assumed. However, mitigation measures should be undertaken as soon as possible to reduce the level to 300 ng/m^3, below which concentrations are thought to be of no concern. Source removal should also be undertaken if levels are found to be between 300 and 3000 ng/m^3 *(8)*.

Neurobehavioural and hormonal effects have been observed in infants exposed to background concentrations of PCBs, prenatally and/or through breastfeeding. The clinical significance of these observations is, however, unclear.

On average, the contribution from inhalation exposure is approximately 1% of the dietary intake but may approach that intake in certain extreme situations (areas close to sources or contaminated indoor air).

Exposures to dioxin-like PCBs can be converted to toxic equivalents using the WHO/IPCS interim toxic equivalent factors *(9)* and subsequently be

assessed using the TDI for TCDD. In 1992, WHO established a TDI for TCDD of 10 pg/kg BW. This was derived on the basis of TCDD-induced liver cancer in rats *(10)* for which a NOAEL of 1 ng/kg BW per day, corresponding to a liver concentration of 540 ng/kg on a wet-weight basis, was calculated. Owing to toxicokinetic differences between humans and rats, this would correspond to a daily intake in humans of 100 pg/kg BW, to which value an uncertainty factor of 10 (to cover inter-individual variation) was applied. Although not explicitly stated, the TDI can be looked on as applicable to the total intake of toxic equivalents derived from PCDDs, PCDFs and other dioxin-like compounds that act by the same mechanisms and cause similar types of toxicity.

For the average consumer, the daily intake of dioxin-like PCBs determined as toxic equivalents would be 10–30% of the TDI. When the contribution from the PCDDs and PCDFs is taken into account, the intake would increase to 20–60%. There are, however, groups with specific dietary habits (such as a high intake of contaminated food) or occupational exposure that may exceed the TDI for PCDDs and PCDFs.

The WHO human milk exposure study *(11)* indicated that the daily intake in toxic equivalents of PCDDs and PCDFs in breastfeeding infants in industrialized countries ranged from about 20 pg/kg BW in less industrialized areas to about 130 pg/kg BW in highly industrialized areas. This indicates intakes 2–13 times higher than the TDI. When the contribution from dioxin-like PCBs is taken into account, the intakes may be up to 2 times higher. It has been noted, however *(12)*, that the TDI should not be applied to such infants because the TDI concept relates to a dose ingested throughout a lifetime. The quantity of PCDDs and PCDFs ingested over a 6-month breastfeeding period would be less than 5% of the quantity ingested over a lifetime.

Guidelines

An air quality guideline for PCBs is not proposed because direct inhalation exposures constitute only a small proportion of the total exposure, in the order of 1–2% of the daily intake from food. WHO has not developed a TDI for total PCB exposure. Owing to the multiplicity of mechanisms underlying PCB-induced health effects, there may not be a scientifically sound rationale to set such a TDI. Average ambient air concentrations of PCBs are estimated to be 3 ng/m^3 in urban areas. Although this air concentration is only a minor contributor to direct human exposure, it is a major contributor to contamination of the food chain. It would also be possible to perform such calculations using toxic equivalents for

dioxin-like PCBs in ambient air, but no such analytical data have been published.

Although indoor air levels of PCBs are generally very low, in certain instances levels of up to several μg/m^3 have been detected. For people living or working in such buildings, exposure to PCBs via air could contribute significantly to the overall PCB exposure.

Because of the potential importance of the indirect contribution of PCBs in air to total human exposure, it is important to control known sources as well as to identify new sources.

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5.11 Polychlorinated dibenzodioxins and dibenzofurans

Exposure evaluation

Food is the main source of human intake of polychlorinated dibenzodioxins (PCDDs) and dibenzofurans (PCDFs); intake through drinking-water is negligible. Calculated as toxic equivalents, average intakes in European countries have been estimated to be in the range 1.5–2 pg/kg body weight (BW) per day *(1–3)*. Very recent data from the Nordic countries indicate that this figure today may be slightly less than 1 pg/kg BW per day *(4, 5)*. For the United States, intake estimates are in the range 1–3 pg/kg BW per day *(6)*.

If the contributions of dioxin-like polychlorinated biphenyls (PCBs) are taken into account, and using the WHO toxic equivalency factors (TEFs) for PCBs *(7, 8)*, the toxic equivalent intake would be in the range 2–6 pg/kg BW per day. For certain risk groups, such as fishermen from the Baltic Sea and Inuits in the Arctic, intakes may be considerably higher.

Inhalation exposure to PCDDs and PCDFs is generally low. Assuming an ambient air toxic equivalent level of 0.1 pg/m^3 and an inhaled volume of air of 20 m^3/day for adults, inhalation intake would amount to about 0.03 pg/kg BW per day *(9, 10)*. Certain industrial and urban areas, however, as well as areas close to major sources, may have up to 20 times higher air concentrations. The contribution to the total toxic equivalents of dioxin-like PCBs from ambient air cannot be calculated owing to lack of congener-specific data. Under special circumstances, for example indoor air highly contaminated from coated particle boards containing PCBs, inhalation exposure may reach 1 pg/kg BW per day *(11)*.

Although present concentrations of PCDDs and PCDFs in ambient air do not present a health hazard through direct human exposure, these concentrations will lead to deposition of PCDDs and PCDFs followed by uptake through the food chain.

Health risk evaluation

In 1990, WHO established a tolerable daily intake (TDI) for TCDD of 10 pg/kg BW *(12)*. This was based on TCDD-induced liver cancer in rats *(13)* for which the NOAEL was 1 ng/kg BW. Owing to toxicokinetic

differences between humans and rats, this corresponded to a daily intake in humans of 100 pg/kg BW, to which value an uncertainty factor of 10 (to cover inter-individual variation) was applied.

Since then, new data on hormonal, reproductive and developmental effects at low doses in animal studies (rats and monkeys) have been published, and the health risk of dioxins was therefore reassessed in 1998 *(14, 15)*. It was concluded that the human data do not lend themselves to be used as the basis for setting a TDI, but they were nevertheless considered to constitute an important reference for comparison with a health risk assessment based on animal data. Consequently, the TDI was based on animal data. It was further decided that body burdens should be used to scale doses across species. Human daily intakes corresponding to body burdens similar to those associated with LOAELS in rats and monkeys could be estimated to be in the range of 14–37 pg/kg BW per day. By applying an uncertainty factor of 10 to this range of LOAELs, a TDI expressed as a range of 1–4 pg toxic equivalent per kg BW was established for dioxins and dioxin-like compounds.

The TDI represents a tolerable daily intake for lifetime exposure, and occasional short-term excursions above the TDI would have no health consequences provided that the averaged intake over long periods was not exceeded. Although not explicitly stated, the TDI can be looked on as applicable to the total intake of toxic equivalents, via both the oral and inhalation routes, derived from PCDDs and PCDFs and other dioxin-like compounds that act by the same mechanisms and cause similar types of toxicity.

The average daily intake by all routes of exposure to PCDDs and PCDFs, calculated as toxic equivalents, is in the same range as the current TDI. When the contribution from dioxin-like PCBs is taken into account, the intake increases by a factor of 2–3. There are, however, groups with specific dietary habits (such as a high intake of contaminated food) or occupational exposure, that may have exposures in excess of the TDI for PCDDs and PCDFs.

The daily intake of PCDDs and PCDFs in breastfed infants in industrialized countries has been calculated in toxic equivalents to range from about 20 pg/kg BW in less industrialized areas up to about 130 pg/kg BW in more industrialized areas. When the contribution from dioxin-like PCBs is taken into account, the intakes may be up to twice these figures. This indicates intakes being far above the TDI. WHO noted, however, that the TDI

should not be applied to breastfed infants because the concept of TDI relates to a dose ingested throughout a lifetime *(14)*. In general, the quantity of PCDDs and PCDFs ingested over a 6-month breastfeeding period would be less than 5% of the quantity ingested over a lifetime.

The contribution from inhalation exposure is on average approximately 1% of the dietary intake, but may in certain extreme situations (areas close to point emission sources or contaminated indoor air) approach the dietary intake.

Guidelines

An air quality guideline for PCDDs and PCDFs is not proposed because direct inhalation exposures constitute only a small proportion of the total exposure, generally less than 5% of the daily intake from food.

Urban ambient toxic equivalent air concentrations of PCDDs and PCDFs are estimated to be about 0.1 pg/m^3. However, large variations have been measured. Although such an air concentration is only a minor contributor to direct human exposure, it is a major contributor to contamination of the food chain. It is difficult, however, to calculate indirect exposure from contamination of food via deposition from ambient air. Mathematical models are being used in the absence of experimental data, but these models require validation. Air concentrations of 0.3 pg/m^3 or higher are indications of local emission sources that need to be identified and controlled.

Although indoor air levels of PCDDs and PCDFs are generally very low, in certain instances, toxic equivalent levels of up to 3 pg/m^3 have been detected. Such levels will constitute an exposure ranging from 25% up to 100% of the current TDI of 1–4 pg toxic equivalent per kg BW (corresponding to 60–240 pg toxic equivalent per day for a 60-kg person).

Owing to the potential importance of the indirect contribution of PCDDs and PCDFs in air to the total human exposure to these compounds through deposition and uptake in the food chain, measures should be undertaken to further reduce emissions to air from known sources. For risk reduction, it is important to control known sources as well as to identify new sources.

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5.12 Styrene

Exposure evaluation

Concentrations of styrene in rural ambient air are generally less than 1 μg/m^3, while indoor air in such locations may contain several μg/m^3. Levels in polluted urban areas are generally less than 20 μg/m^3 but can be much higher in newly built houses containing styrene-based materials.

Health risk evaluation

Potentially critical effects for the derivation of a guideline for styrene are considered to be carcinogenicity/genotoxicity and neurological effects, including effects on development.

Styrene in its pure form has an odour detection threshold of 70 μg/m^3. Its pungent odour is recognized at concentrations three to four times greater than this threshold value.

The value of the available evidence for an association between exposure to styrene and small increases in lymphatic and haematopoietic cancers observed in workers in some studies is limited by concurrent exposure to other substances, lack of specificity and absence of dose–response. In limited studies in animals, there is little evidence that styrene is carcinogenic. IARC has classified styrene in group 2B *(1)*.

Styrene was genotoxic *in vivo* and *in vitro* following metabolic activation. In cytogenetic studies on peripheral lymphocytes of workers in the reinforced plastics industry, there were increased rates of chromosomal aberrations at mean levels of styrene of more than 120 mg/m^3 (> 20 ppm). Elevated levels of single-strand breaks and styrene-7,8-oxide adducts in DNA and haemoglobin have also been observed. Although these genotoxic effects have been observed at relatively low concentrations, they were not considered as critical endpoints for development of a guideline, in view of the equivocal evidence of carcinogenicity for styrene.

The available data, although limited, indicate that neurotoxicity in the form of neurological developmental impairments is among the most sensitive of endpoints. In the offspring of rats exposed to styrene at a concentration of 260 mg/m^3 (60 ppm) there were effects on behaviour and biochemical parameters in the brain *(2)*.

Guidelines

Although genotoxic effects in humans have been observed at relatively low concentrations, they were not considered as critical endpoints for development of a guideline, in view of the equivocal evidence for the carcinogenicity of styrene.

In occupationally exposed populations, subtle effects such as reductions in visuomotor accuracy and verbal learning skills *(3–5)* and subclinical effects on colour vision have been observed at concentrations as low as 107–213 mg/m^3 (25–50 ppm) *(6–10)*. Taking the lower number of this range for precautionary reasons, adjusting this to allow for conversion from an occupational to a continuous pattern of exposure (a factor of 4.2), and incorporating a factor of 10 for inter-individual variation and 10 for use of a LOAEL rather than a NOAEL results in a guideline of 0.26 mg/m^3 (weekly average). This value should also be protective for the developmental neurological effects observed in animal species.

The air quality guideline could also be based on the odour threshold. In that case, the peak concentration of styrene in air should be kept below the odour detection threshold level of 70 µg/m^3 as a 30-minute average.

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5.13 Tetrachloroethylene

Exposure evaluation

Ambient air concentrations of tetrachloroethylene are generally less than 5 μg/m^3 in urban areas and typically less than 1 μg/m^3 in rural areas. Indoor concentrations are generally less than 5 μg/m^3. Indoor tetrachloroethylene air levels may rise to more than 1 mg/m^3 in close proximity to dry-cleaning operations where tetrachloroethylene is used as a cleaning solvent or in homes where dry-cleaned clothing is often worn. Inhalation of tetrachloroethylene is the major route of exposure in the general population.

Health risk evaluation

The main health effects of concern are cancer and effects on the central nervous system, liver and kidneys. Tetrachloroethylene is classified by IARC as a Group 2A carcinogen (probably carcinogenic to humans) *(1)*.

In carcinogenicity studies, an increased incidence of adenomas and carcinomas was observed in the livers of exposed mice. There is suggestive evidence from mechanistic studies that humans are less sensitive to the development of these tumours following tetrachloroethylene exposure. A low incidence of kidney tumours has been reported among male rats. It can be concluded from this small and statistically non-significant increase, together with the data related to a possible mechanism of induction, that the result in male rats is equivocal evidence only for a risk of renal cancer in humans. The significance for humans of the increased incidences of mononuclear-cell leukaemias, as observed in a study in F344 rats, is unclear owing to the lack of understanding of the mechanism underlying the formation of this cancer type, which has a high background incidence.

Epidemiological studies in humans show positive associations between exposure to tetrachloroethylene and risks for oesophageal and cervical cancer and non-Hodgkin lymphoma. Confounding factors cannot be ruled out and the statistical power of the studies is limited. These studies therefore provide only limited evidence for the carcinogenicity of tetrachloroethylene in humans *(1)*.

From the weight of the evidence from mutagenicity studies, it can be concluded that tetrachloroethylene is not genotoxic. Several *in vitro* studies indicate that conjugation of tetrachloroethylene with reduced glutathione, a minor biotransformation route demonstrated to occur in rodents,

produces renal metabolites that are mutagenic in *Salmonella typhimurium* TA 100 *(1)*. In the absence of further data on this point, the significance of the latter results for humans is uncertain.

Short-term exposure studies in volunteers (duration 1 or 5 days) have shown effects on the central nervous system at a concentration of > 678 mg/m^3 *(2–5)*. A recent study of dry-cleaning workers with long-term exposure showed that renal effects may develop at lower exposure concentrations, with the reported onset of renal damage occurring following exposure to a median concentration of 102 mg/m^3 (range, trace to 576 mg/m^3) *(6)*.

Although the results of carcinogenicity studies in experimental animals are available, those of adequate long-term toxicity studies are not. A chronic LOAEL of 678 mg/m^3 (100 ppm) for the systemic toxicity (in kidney and liver) of tetrachloroethylene in mice can be derived from the National Toxicology Program carcinogenicity study in this species *(7)*.

Use of existing physiologically based pharmacokinetic models for derivation of a guideline value based on kidney effects is not considered feasible because these models do not contain the kidney or kidney-specific metabolism as a component. As yet it is therefore unknown what an appropriate internal dose measure would be.

Guidelines

Given the limitations of the weight of the epidemiological evidence, and the uncertainty of the relevance to humans of the induction of tumours in animals exposed to tetrachloroethylene, the derivation of a guideline value is at present based on non-neoplastic effects rather than on carcinogenicity as the critical endpoint.

On the basis of a long-term LOAEL for kidney effects of 102 mg/m^3 in dry-cleaning workers, a guideline value of 0.25 mg/m^3 is calculated. In deriving this guideline value, the LOAEL is converted to continuous exposure (dividing by a factor of 4.2, 168/40) and divided by an uncertainty factor of 100 (10 for use of an LOAEL and 10 for intraspecies variation). Recognizing that some uncertainty in the LOAEL exists because the effects observed at this level are not clear-cut, and because of fluctuations in exposure levels, an alternative calculation was made based on the LOAEL in mice of 680 mg/m^3, and using an appropriate uncertainty factor of 1000. This calculation yields a guideline value of 0.68 mg/m^3.

On the basis of the overall health risk evaluation, a guideline of 0.25 mg/m^3 is currently established. However, the concern about a possible carcinogenic effect of tetrachloroethylene exposure in humans should be addressed through in-depth risk evaluation in the near future.

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5.14 Toluene

Exposure evaluation

Mean ambient air concentrations of toluene in rural areas are generally less than 5 μg/m^3, while urban air concentrations are in the range 5–150 μg/m^3. Concentrations may be higher close to industrial emission sources.

Health risk evaluation

Toluene in its pure form has an odour detection threshold of 1 mg/m^3 (*1, 2*). Its odour is recognized at concentrations about ten times greater than this threshold value (*1–3*).

The acute and chronic effects of toluene on the central nervous system are the effects of most concern. Toluene may also cause developmental decrements and congenital anomalies in humans, and these effects are supported by findings of studies on animals, for example fetal development retardation, skeletal anomalies, low birth weight and developmental neurotoxicity. The potential effects of toluene on reproduction and hormone balance in women, coupled with findings of hormone imbalances in exposed males, are also of concern. Limited information suggests an association between occupational toluene exposure and spontaneous abortions. Both the human and animal data indicate that toluene is ototoxic at elevated exposures. Sensory effects have also been found. Toluene has minimal effects on the liver and kidney, except in cases of toluene abuse. There has been no indication that toluene is carcinogenic in bioassays conducted to date, and the weight of available evidence indicates that it is not genotoxic.

The lowest level of chronic occupational toluene exposure unequivocally associated with neurobehavioural functional decrements is 332 mg/m^3 (88 ppm) *(4, 5)*. Effects on the central nervous system in humans are supported by findings in exposed animals. For example, rat pups exposed to either 100 or 500 ppm 1–28 days after birth demonstrated histo-pathological changes in the hippocampus *(6)*. Women occupationally exposed to toluene at an average concentration of 332 mg/m^3 (88 ppm) incurred higher spontaneous abortion rates and menstrual function disturbances *(7–9)*. The interpretation of these observations was hampered, however, by confounding factors *(10)*. Men occupationally exposed to toluene at 5–25 ppm have also been shown to exhibit hormonal changes.

With regard to short-term exposure, subjective effects have been reported at 100 ppm (6-hour exposure) while symptoms at lower levels cannot be ruled out. Numerous confounding factors, however, need to be considered.

Exposure data related to central nervous system endpoints were best characterized in certain occupational studies and these data have been employed in the derivation of the guideline. A NOAEL for chronic effects of toluene has not been identified.

Guidelines

The LOAEL for effects on the central nervous system from occupational studies is approximately 332 mg/m^3 (88 ppm). A guideline value of 0.26 mg/m^3 is established from these data, adjusting for continuous exposure (dividing by a factor of 4.2) and dividing by an uncertainty factor of 300 (10 for inter-individual variation, 10 for use of a LOAEL rather than a NOAEL, and an additional factor of 3 given the potential effects on the developing central nervous system). This guideline value should be applied as a weekly average. This guideline value should also be protective for reproductive effects (spontaneous abortions).

The air quality guideline could also be based on the odour threshold. In this case, the peak concentrations of toluene in air should be kept below the odour detection threshold level of 1 mg/m^3 as a 30-minute average.

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5.15 Trichloroethylene

Exposure evaluation

The average ambient air concentrations of trichloroethylene are less than 1 µg/m^3 in rural areas and up to 10 µg/m^3 in urban areas. Concentrations in indoor air are typically similar, although higher concentrations can be expected in certain areas, such as in proximity to industrial operations. Inhalation of airborne trichloroethylene is the major route of exposure for the general population.

Health risk evaluation

The main health effects of concern with trichloroethylene are cancer, and effects on the liver and the central nervous system.

Studies in animals and humans show that the critical organs or systems for noncarcinogenic effects are the liver and the central nervous system. The dose–response relationship for these effects is insufficiently known, making it difficult to assess the health risk for the occurrence of these effects in case of long-term exposure to low levels of trichloroethylene.

IARC has classified trichloroethylene as a Group 2A carcinogen (probably carcinogenic to humans). This classification was based on sufficient evidence in animals and limited evidence in humans *(1)*.

The available data suggest that trichloroethylene may have a weak genotoxic action *in vivo*. Several of the animal carcinogenicity studies show limitations in design. In mice, increased incidences of adenomas and carcinomas in lungs and liver were observed *(2–5)*. In two rat studies, the incidence of testicular tumours was increased *(6, 7)*. Evidence from mechanistic studies suggests that humans are likely to be less susceptible to developing tumours as a result of exposure to trichloroethylene. Nevertheless, the relevance of the observed increase in lung tumours in mice and testicular tumours in rats for human cancer risks cannot be excluded. The results of the mechanistic studies do not provide full elucidation or guidance on this point.

Positive associations between exposure to trichloroethylene and risks for cancer of the liver and biliary tract and non-Hodgkin lymphomas were observed in epidemiological studies on cancer in humans. Confounding cannot be ruled out. A quantitative risk estimate cannot be made from these human data. The increased tumours in lungs and testes observed in animal

bioassays are considered to be the best available basis for the risk evaluation. However, it cannot be conclusively established whether a threshold with regard to carcinogenicity in the action of trichloroethylene may be assumed. Therefore, linear extrapolation from the animal tumour data is used, providing a conservative approach to the estimation of human cancer risk.

Using the data on the incidence of pulmonary adenomas in B3C6F1 mice and on pulmonary adenomas/carcinomas in Swiss mice *(2)*, unit risks of 9.3×10^{-8} and 1.6×10^{-7}, respectively, can be calculated by applying the linearized multistage model. Applying the same model on the incidence of Leydig cell tumours in the testes of rats, a unit risk of 4.3×10^{-7} can be derived *(6)*.

Physiologically based pharmacokinetic models have been developed for trichloroethylene. Use of these models for cancer risk estimates is not considered feasible because it is not known what an appropriate internal dose measure would be.

Guidelines

Because the available evidence indicates that trichloroethylene is genotoxic and carcinogenic, no safe level can be recommended. On the basis of the most sensitive endpoint, Leydig cell tumours in rats, a unit risk estimate of 4.3×10^{-7} per $\mu g/m^3$ can be derived. The ranges of ambient air concentrations of trichloroethylene corresponding to an excess lifetime risk of 1:10 000, 1:100 000 and 1:1 000 000 are 230, 23 and 2.3 $\mu g/m^3$, respectively.

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5.16 Vinyl chloride

Exposure evaluation

Calculations based on dispersion models indicate that 24-hour average concentrations of 0.1–0.5 μg/m^3 exist as background levels in much of western Europe, but such concentrations are below the current detection limit (approximately 1.0 μg/m^3). In the vicinity of vinyl chloride (VC) and polyvinyl chloride (PVC) production facilities 24-hour concentrations can exceed 100 μg/m^3, but are generally less than 10 μg/m^3 at distances greater than 1 km from plants. The half-time of VC in the air is calculated to be 20 hours; this figure is based on measured rates of reaction with hydroxyl radicals and their concentrations in the air *(1)*.

Health risk evaluation

There is sufficient evidence of carcinogenicity of VC in humans and experimental animals *(2)*. Extrapolation (or rather interpolation) to lower exposure levels can be made, based on knowledge or assumptions about the dose and time-dependence of risk. As seen in the low exposure data of Maltoni et al. *(3)*, a linear dose–response relationship accords well with the animal data for haemangiosarcoma. The finding of at least three cases of haemangiosarcoma in PVC processors as compared with about 100 in VC or PVC production workers is compatible with a linear relationship. The average exposures in the production industry were about 100 times lower than those in the polymerization industry, but the workforce was 10 times larger.

Data from a cohort study *(4)* and an analysis of the incidence of haemangiosarcoma in the United States and western Europe *(5)* suggest that the risk of haemangiosarcoma increases as the second or third power of time from onset of exposure. Using a model in which the risk increases as t^3 during exposure and as t^2 subsequently, estimates of the relative risk in various exposure circumstances can be calculated and used to convert limited-duration exposure risks into lifetime exposure risks.

Estimates of cancer risk can be made from the data relating to the cohort studied by Nicholson et al. *(4)*. A group of 491 workers at two long-established PVC production plants was studied. One plant began operations in 1936 and the other in 1946. Each cohort member had a minimum of 5 years' employment; the average work duration was 18 years. It is estimated that the average VC exposure was 2050 mg/m^3. The overall

standardized mortality rate (SMR) for cancer was 142 (28 observed; 19.7 expected); that for liver and biliary cancer was 2380 (10 observed; 0.42 expected). Using the liver cancer data, the estimated lifetime risk of death from VC exposure is 3.6×10^{-4} per mg/m^3, or [(23.8–1) × 0.003/(2050 mg/m^3) × 2.8 × 70/18], where 0.003 is the lifetime risk of death from liver biliary cancer in white American males, 2.8 is the working week–total week conversion and 70/18 the work period–lifetime conversion. Since there are an equal number of cancers at other sites (averaging over 12 cohorts), the excess cancer risk is 7.2×10^{-4} per mg/m^3. If the total cancer SMR is used directly, the risk is 4.5×10^{-4} per mg/m^3, or [(1.42–1) × 0.2/(2050 mg/m^3) × 2.8 × 70/18], which is in good agreement with the above. The average of the two estimates indicates that a 10^{-6} cancer risk occurs at exposures of 1.7 μg/m^3.

The risk of cancer from VC can be calculated from data on the United States population exposed in the Equitable Environmental Health study *(6).* This study identified 10 173 workers who were employed for one or more years in 37 (of 43) VC and PVC production plants. The average duration of employment before 1973 was 8.7 years. Using the data of Barnes *(7),* a weighted exposure of 650 ppm (1665 mg/m^3) was estimated. Considering the total population at risk to be 12 000, the unit exposure lifetime risk from an average exposure of 9 years is $0.75 \times l0^{-5}$ per mg/m^3, or [(150/12 000) × (1/1665)].

Using a linear dose–response relationship converting to a lifetime exposure (assuming that one half of the workers began exposure at the age of 20 and one half at the age of 30), the continuous lifetime haemangiosarcoma risk is 4.7×10^{-4} per mg/m^3, or [$0.75 \times 10^{-5} \times 2.8 \times 22.4$], where 2.8 is the ratio of the air volume inhaled in a full week (20 m^3 × 7) to that in a working week (10 m^3 × 5) and 22.4 is the average conversion to a lifetime for a ten-year exposure beginning at an average age of 25 years, taking into account the time course of haemangiosarcoma. (Without explicit consideration of the time course, the multiplier would be 70/9 = 7.8.) A 10^{-6} risk occurs at a concentration of 2.1 μg/m^3.

Assuming that the number of cancers in other sites may equal that of haemangiosarcomas, the best estimate for excess cancer risk is that a 10^{-6} risk occurs as a result of continuous lifetime exposure to 1.0 μg/m^3.

The risks estimated from epidemiological studies are the most relevant for human exposures. The above estimate from human angiosarcoma incidences is a conservative one from the point of view of health, because of the use of

a model that assumes that the haemangiosarcoma risk continues to increase throughout the lifetime of an exposed individual.

These risk estimates are in agreement with those made by others. The US Environmental Protection Agency has estimated that 11 cancer deaths per year would result from 4.6×10^{-6} people being exposed to 0.017 ppm (43 μg/m^3) *(8)*: this translates to a 10^{-6} lifetime risk at 0.25 μg/m^3. A Dutch criteria document, on the basis of animal data, estimates that a 10^{-6} risk occurs at 0.035 μg/m^3 *(1)*.

One cautionary note should be sounded: the particular sensitivity of newborn rats to VC, referred to above, suggests that risks may be much greater in childhood than those estimated from adult exposures. By the age of 10 years, however, the latter risks should prevail.

Guidelines

Vinyl chloride is a human carcinogen and the critical concern with regard to environmental exposures to VC is the risk of malignancy. No safe level can be indicated. Estimates based on human studies indicate a lifetime risk from exposure to 1 μg/m^3 to be 1×10^{-6}.

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CHAPTER 6

Inorganic pollutants

6.1 Arsenic

Exposure evaluation

There are many arsenic compounds, both organic and inorganic, in the environment. Airborne concentrations of arsenic range from 1 ng/m^3 to 10 ng/m^3 in rural areas and from a few nanograms per cubic metre to about 30 ng/m^3 in noncontaminated urban areas. Near emission sources, such as nonferrous metal smelters and power plants burning arsenic-rich coal, concentrations of airborne arsenic can exceed 1 µg/m^3.

Health risk evaluation

Inorganic arsenic can have acute, subacute and chronic effects, which may be either local or systemic. Lung cancer is considered to be the critical effect following inhalation. An increased incidence of lung cancer has been seen in several occupational groups exposed to inorganic arsenic compounds. Some studies also show that populations near emission sources of inorganic arsenic, such as smelters, have a moderately elevated risk of lung cancer. Information on the carcinogenicity of arsenic compounds in experimental animals was considered inadequate to make an evaluation *(1, 2)*.

A significant number of studies concerning occupational exposure to arsenic and the occurrence of cancer have been described. Unit risks derived by the US Environmental Protection Agency (EPA) Carcinogen Assessment Group in 1984 *(3)* were not changed until 1994 *(4)*. They form five sets of data involving two independently exposed populations of workers in Montana and Tacoma smelters in the United States, ranging from 1.25×10^{-3} to 7.6×10^{-3}, a weighted average of these five estimates giving a composite estimate of 4.29×10^{-3}.

A WHO Working Group on Arsenic *(5)* conducted a quantitative risk assessment, assuming a linear relationship between the cumulative arsenic dose and the relative risk of developing lung cancer. Risk estimates for lung cancer from inorganic arsenic exposure were based on the study by Pinto et al. *(6)* of workers at the Tacoma smelter. The lifetime risk of lung cancer was calculated to be 7.5×10^{-3} per microgram of airborne arsenic per cubic metre.

The second study relating to the quantitative risk assessment included a large number of the 8047 males employed as smelting workers at the Montana copper smelter *(7)*. Exposures to airborne arsenic levels were estimated to average 11.17, 0.58 and 0.27 mg/m^3 in the high-, medium- and

low-exposure areas. Unit risks for these three groups were calculated to be 3.9×10^{-3}, 5.1×10^{-3} and 3.1×10^{-3}, respectively.

Assuming that the risk estimation based on the Tacoma study was higher because of the urine measurements made, it may have underestimated the actual inhalation exposure; the unit risk was considered to be 4×10^{-3}.

In 1994, Viren & Silvers *(8)*, using updated results from the cohort mortality study in the Tacoma smelter workers together with findings from a cohort study of 3619 Swedish smelter workers, developed other unit risk estimates. A unit risk of 1.28×10^{-3} was estimated for the Tacoma smelter cohort and 0.89×10^{-3} for the Swedish cohort. Pooling these new estimates with the EPA's earlier estimates from the Montana smelter yielded a composite unit risk of 1.43×10^{-3} (Table 13). This value is three times lower than the EPA estimate *(4)* and two times lower than the value assumed in the first edition of *Air quality guidelines for Europe (9)*.

Table 13. Updated unit risk estimates

Risk update	Smelter population	Estimated unit risk: Study	Estimated unit risk: Cohort	Estimated unit risk: Pooled
Pooled estimate using updated Swedish and Tacoma cohorts	Tacoma, 1987	1.28×10^{-3}	1.28×10^{-3}	1.07×10^{-3}
	Ronnskar, 1989:			
	– workers hired pre-1940	0.46×10^{-3}	0.89×10^{-3}	
	– workers hired 1940 and later	1.71×10^{-3}	—	
Updated Tacoma cohort with original EPA estimates for Montana cohort	Tacoma, 1987 (updated results supersede earlier estimates)		1.28×10^{-3}	1.81×10^{-3}
	Montana, 1984 (new estimates not available, 1984 EPA estimates apply)		2.56×10^{-3}	
Pooled across all smelter cohorts	Ronnskar, 1989		0.89×10^{-3}	1.43×10^{-3}
	Tacoma, 1987		1.28×10^{-3}	
	Montana, 1984		2.56×10^{-3}	

Source: Viren & Silvers *(8)*.

Guidelines

Arsenic is a human carcinogen. Present risk estimates have been derived from studies in exposed human populations in Sweden and the United States. When assuming a linear dose–response relationship, a safe level for inhalation exposure cannot be recommended. At an air concentration of 1 μg/m^3, an estimate of lifetime risk is 1.5×10^{-3}. This means that the excess lifetime risk level is 1:10 000, 1:100 000 or 1:1 000 000 at an air concentration of about 66 ng/m^3, 6.6 ng/m^3 or 0.66 ng/m^3, respectively.

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6.2 Asbestos

Exposure evaluation

Actual indoor and outdoor concentrations in air range from below one hundred to several thousand fibres per m^3.

Health risk evaluation

On the basis of the evidence from both experimental and epidemiological studies, it is clear that asbestos inhalation can cause asbestosis, lung cancer and mesothelioma. The evidence that ingested asbestos causes gastrointestinal or other cancers is insufficient. Furthermore, the carcinogenic properties of asbestos are most probably due to its fibre geometry and remarkable integrity; other fibres with the same characteristics may also be carcinogenic.

Current environmental concentrations of asbestos are not considered a hazard with respect to asbestosis. However, a risk of mesothelioma and lung cancer from the current concentrations cannot be excluded.

In 1986 a WHO Task Group expressed reservations about the reliability of risk assessment models applied to asbestos risk. Its members suggested that such models can only be used to obtain a broad approximation of the lung cancer risk of environmental exposures to asbestos and "that any number generated will carry a variation over many orders of magnitude". The same was found to be true for estimates of the risk of mesothelioma. The same document stated: "In the general population the risks of mesothelioma and lung cancer attributable to asbestos cannot be quantified reliably and probably are undetectably low." *(1)*.

The following estimates of risk are based on the relatively large amount of evidence from epidemiological studies concerning occupational exposure. Data from these studies have been conservatively extrapolated to the much lower concentrations found in the general environment. Although there is evidence that chrysotile is less potent than amphiboles, as a precaution chrysotile has been attributed the same risk in these estimates.

Mesothelioma

A formula by which the excess incidence of mesothelioma can be approximated has been derived by Peto *(2)*. Fibre concentration, duration of exposure and time since first exposure are parameters incorporated in this model, which assumes a linear dose–response relationship. Peto verified this model

from data on an urban population exposed for its whole life and on workers exposed for many decades. In both cases, duration of exposure is assumed to be equal or close to time since first exposure. The data show that the incidence of mesothelioma is proportional to the fibre concentration to which the workers were exposed and to time since first exposure for both workers and the general population. Starting from this relationship, one may calculate the risk of lifetime exposure to environmental concentrations from the incidence of mesothelioma in occupational populations exposed to much higher concentrations, but for a shorter time.

Apart from incomplete knowledge about the true workplace exposure, a further complication arises from the fact that workplace concentrations were measured by means of an optical microscope, counting only fibres longer than 5 µm and thicker than, say, 0.5 µm. In this chapter all fibre concentrations based on optical microscopy are marked F*/m^3 and risk estimates will be based on F*/m^3. If concentrations measured by optical microscopy are to be compared with environmental fibre concentrations measured by scanning electron microscopy, a conversion factor has to be used: 2 F/m^3 = 1 F*/m^3.

Several studies have been performed to calculate the risk of mesothelioma resulting from nonoccupational exposure to asbestos. Lifetime exposure to 100 F*/m^3 has been estimated by various authors to carry differing degrees of mesothelioma risk (see Table 14). The risk estimates in Table 14 differ by a factor of 4. A "best" estimate may be 2×10^{-5} for 100 F*/m^3.

An independent check of this risk estimate can be made by calculating the incidence of mesothelioma in the general population, based on a hypothetical

Table 14. Estimates of mesothelioma risk resulting from lifetime exposure to asbestos

Risk of mesothelioma from 100 F*/m^3	Values in original publication (risk for fibre concentration indicated)	Reference
1.0×10^{-5}	1.0×10^{-4} for 1000 F*/m^3	*(3)*
~2.0×10^{-5}	1.0×10^{-4} for (130–800) F*/m^3	*(4)*
~3.9×10^{-5}	1.56×10^{-4} for 400 F*/m^3	*(5, 6)*
~2.4×10^{-5}	2.75×10^{-3} (females), 1.92×10^{-3} (males) } for 0.01 F/ml	*(7)*

average asbestos exposure 30–40 years ago *(8)*. If the latter had been 200–500 F*/m^3 (corresponding to about 400–1000 F/m^3 as measured today), the resulting lifetime risk of mesothelioma would be (4–10) × 10^{-5}. With the average United States death rate of 9000 × 10^{-6} per year, this would give 0.4–0.9 mesothelioma cases each year per million persons from past environmental asbestos exposure. The reported mesothelioma incidence in the United States ranges from 1.4 × 10^{-6} per year to 2.5 × 10^{-6} per year according to various authors *(5, 8)*. Thus, the calculated risk figures would account for only part of the observed incidence. Nevertheless, other factors that may account for this discrepancy must be considered.

- Uncertainties in the risk extrapolations result from the lack of reliable exposure data in the cohort studies, errors in the medical reports, and necessary simplifications in the extrapolation model itself *(7)*. Furthermore, the amount of past ambient exposure can only be an educated guess.

- The incidence of nonoccupational mesotheliomas is calculated from the difference between the total of observed cases and the number of those probably related to occupational exposure. Neither of these two figures is exactly known. Moreover, the influence of other environmental factors in the generation of mesothelioma is unknown.

In the light of these uncertainties, the result obtained by using the risk estimate can be considered to be in relatively good agreement with the annual mesothelioma death rate based on national statistical data.

Lung cancer

Unlike mesothelioma, lung cancer is one of the most common forms of cancer. As several exogenous noxious agents can be etiologically responsible for bronchial carcinoma, the extrapolation of risk and comparison between different studies is considerably complicated. In many epidemiological studies, the crucial effect of smoking has not been properly taken into account.

Differentiation of the observed risks according to smoking habits has been carried out, however, in the cohort of North American insulation workers studied by Hammond et al. *(9)*. This study suggests that the relative risk at a given time is approximately proportional to the cumulative amount of fine asbestos dust received up to this point, for both smokers and nonsmokers. The risks for non-asbestos-exposed nonsmokers and smokers must therefore be multiplied by a factor that increases in proportion to the cumulative exposure.

The dose–response relationship in the case of asbestos-induced lung cancer can be described by the following equation *(7)*.

$$I_L \text{ (age, smoking, fibre dose)} = I_L^o \text{ (age, smoking)}[1 + K_L \times C_f \times d]$$

This equation could also be written as:

$$K_L = [(I_L/I_L^o) - 1]/C_f \times d = (\text{relative risk} - 1)/(\text{cumulative exposure})$$

where:

K_L = a proportionality constant, which is a measure of the carcinogenic potency of asbestos

C_f = fibre concentration

d = duration of exposure in years

I_L = lung cancer incidence, observed or projected, in a population exposed to asbestos concentration C_f during time d

I_L^o = lung cancer incidence expected in a group without asbestos exposure but with the same age and smoking habits (this factor includes age dependence).

There are several studies that allow the calculation of K_L. Liddell *(10, 11)* has done this in an interesting and consistent manner. The results are given in Table 15.

Taking the data in Table 15 as a basis, a reasonable estimate for K_L is 1.0 per 100 F*years/ml. For a given asbestos exposure, the risk for smokers is about 10 times that for nonsmokers *(9)*. In extrapolating from workers to the general public, a factor of 4 for correction of exposure time has to be applied to K_L.

The incidence of lung cancer in the general population exposed to 100 F*/m^3 is calculated as follows:

$$I_L = I_L^o(1 + 4 \times 0.01 \times 10^{-4} \text{ F*/ml} \times 50 \text{ years})$$

or

$$I_L = I_L^o(1 + 2 \times 10^{-4} \text{ F*/ml})$$

Table 15. Increase in the relative risk of lung cancer, as shown by different studies

K_L per 100 F*year/ml	Type of activity	Reference
0.04	mining and milling	*(12)*
0.045	mining and milling	*(13)*
0.06	friction material	*(14)*
0.1	factory processes	*(15, 16)*
(M) 0.4–1.1	factory processes	
(F) 2.7 [a]	factory processes	*(17)*[b]
0.2	asbestos-cement	*(18)*
0.07	textiles (before 1951)	*(19)*
0.8 [a]	textiles (after 1950)	
6(M) 1.6 [a]	textiles	*(20)*
1.6	textiles	*(21)*[c]
1.1	insulation products	*(22)*[b]
1.5	insulation	*(23)*[b]

[a] Fewer than 10 cases of lung cancer expected (i.e. small cohort).

[b] Inadequate knowledge of actual fibre concentrations.

[c] Same factory as in *(20)*, but larger cohort.

Source: Liddell *(10)*.

The extra risk is $I_L - I_L^o$. Values for I_L^o are about 0.1 for male workers and 0.01 for male nonsmokers *(5)*.

Lifetime exposure to 100 F*/m^3 (lifetime assumed to be 50 years since, in a lifetime of 70 years, the first 20 years without smoking probably do not make a large contribution) is therefore estimated as follows.

Status	Risk of lung cancer per 100 000	Range (using the highest and lowest values of K_L from Table 15)
Smokers	2.0	0.08–3.2
Nonsmokers	0.2	0.008–0.32

This risk estimate can be compared, when adjusted to 100 F*/m^3, with estimates for male smokers made by other authors or groups:

Breslow (National Research Council) *(6)*: 7.3×10^{-5}

Schneiderman et al. *(4)*: $(14–1.4) \times 10^{-5}$

US Environmental Protection Agency *(7)*: 2.3×10^{-5}.

A fibre concentration of 100 F*/m^3 (about 200 F/m^3 as seen by scanning electron microscope) thus gives a total risk of $(2 + 2) \times 10^{-5}$ for smokers or 2.2×10^{-5} for nonsmokers.

Guidelines

Asbestos is a proven human carcinogen (IARC Group 1). No safe level can be proposed for asbestos because a threshold is not known to exist. Exposure should therefore be kept as low as possible.

Several authors and working groups have produced estimates indicating that, with a lifetime exposure to 1000 F/m^3 (0.0005 F*/ml or 500 F*/m^3, optically measured) in a population of whom 30% are smokers, the excess risk due to lung cancer would be in the order of 10^{-6}–10^{-5}. For the same lifetime exposure, the mesothelioma risk for the general population would be in the range 10^{-5}–10^{-4}. These ranges are proposed with a view to providing adequate health protection, but their validity is difficult to judge. An attempt to calculate a "best" estimate for the lung cancer and mesothelioma risk is described above.

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6.3 Cadmium

Exposure evaluation

It is not possible to carry out a dose–response analysis for cadmium in air solely on the basis of epidemiological data collected in the general population, since the latter is exposed to cadmium mainly via food or tobacco smoking. In addition, the recently reported renal effects in areas of Belgium and the Netherlands polluted by cadmium refer to historical contamination of the environment. Assuming, however, that the only route of exposure is by inhalation, an indirect estimate of the risk of renal dysfunction or lung cancer can be made on the basis of data collected in industrial workers.

Health risk evaluation

Pooled data from seven studies, in which the relationships between the occurrence of tubular proteinuria and cumulative cadmium exposure were examined, show that the prevalence of tubular dysfunction (background level 2.4%) increases sharply at a cumulative exposure of more than 500 μg/m^3-years (8% at 400 μg/m^3-years, 50% at 1000 μg/m^3-years and > 80% at more than 4500 μg/m^3-years) *(1)*. Some studies suggest that a proportion of workers with cumulative exposures of 100–400 μg/m^3-years might develop tubular dysfunction (prevalences increasing from 2.4% to 8.8%, at cumulative exposures above 200 μg/m^3-years). These estimates agree well with that derived from the kinetic model of Kjellström *(2),* which predicted that the critical concentration of 200 mg/kg in the renal cortex will be reached in 10% of exposed workers after 10 years of exposure to 50 μg/m^3 and in 1% after 10 years of exposure to 16 μg/m^3 (cumulative exposures of 500 and 160 μg/m^3-years, respectively).

With respect to the risk of lung cancer, two risk estimates have been made, one based on the long-term rat bioassay data of Takenaka et al. *(3)* and the other on the epidemiological data of Thun et al. *(4)*. Modelling of these data yielded risk estimates that did not agree. On the basis of the Takenaka data, the unit risk is 9.2×10^{-2} per μg/m^3; the human data yielded a unit risk of 1.8×10^{-3} per μg/m^3. In general, the use of human data is more reliable because of species variation in response. Nevertheless, there is evidence from recent studies that this latter unit risk might be substantially overestimated owing to confounding by concomitant exposure to arsenic.

Some uncertainty exists with regard to the thresholds of exposure associated with effects on the kidney. This is primarily due to the limited number

of subjects, methodological differences and inaccuracies in exposure data. An overall assessment of the data from industrial workers suggests that, to prevent tubular dysfunction, the 8-hour exposure level for cadmium should not exceed 5 μg/m^3. This corresponds to a cumulative exposure of 225 μg/m^3-years. Adopting the lowest estimate of the critical cumulative exposure to airborne cadmium (100 μg/m^3-years), extrapolation to continuous lifetime exposure results in a permissible concentration of about 300 ng/m^3.

Cadmium in ambient air is transferred to soil by wet or dry deposition and can enter the food chain. However, the rate of transfer from soil to plant depends on numerous factors (type of soil and plant, soil pH, use of fertilizers, meteorology, etc.) and is impossible to predict.

Present average concentrations of cadmium in the renal cortex in the general population in Europe at the age of 40–60 years are in the range 15–40 mg/kg. These values are only 4–12 times lower than the critical levels estimated in cadmium workers for the induction of tubular dysfunction (180 mg/kg) and very close to the critical level of 50 mg/kg estimated by the Cadmibel study in Belgium *(5)*. Any further increase in the dietary intake of cadmium owing to an accumulation of the metal in agricultural soils will further narrow the gap to these critical levels. It is thus imperative to maintain a zero balance for cadmium in agricultural soils by controlling and restricting inputs from fertilizers (including sewage sludge) and atmospheric emissions. Since emissions from industry are currently decreasing, attention must be focused on the emissions from waste incineration, which are likely to increase in the future.

Guidelines

IARC has classified cadmium and cadmium compounds as Group 1 human carcinogens, having concluded that there was sufficient evidence that cadmium can produce lung cancers in humans and animals exposed by inhalation *(6)*. Because of the identified and controversial influence of concomitant exposure to arsenic in the epidemiological study, however, no reliable unit risk can be derived to estimate the excess lifetime risk for lung cancer.

Cadmium, whether absorbed by inhalation or via contaminated food, may give rise to various renal alterations. The lowest estimate of the cumulative exposure to airborne cadmium in industrial workers leading to an increased risk of renal dysfunction (low-molecular-weight proteinuria) or lung cancer is 100 μg/m^3-years for an 8-hour exposure. Extrapolation to a

continuous lifetime exposure gives a value of around 0.3 μg/m^3. Existing levels of cadmium in the air of most urban or industrial areas are around one-fiftieth of this value.

The finding of renal effects in areas contaminated by past emissions of cadmium indicates that the cadmium body burden of the general population in some parts of Europe cannot be further increased without endangering renal function. To prevent any further increase of cadmium in agricultural soils likely to increase the dietary intake of future generations, a guideline of 5 ng/m^3 is established.

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6.4 Chromium

Exposure evaluation

Chromium is ubiquitous in nature. Available data, generally expressed as total chromium, show a concentration range of 5–200 ng/m^3. There are few valid data on the valency and bioavailability of chromium in the ambient air.

Health risk evaluation

Chromium(III) is recognized as a trace element that is essential to both humans and animals. Chromium(VI) compounds are toxic and carcinogenic, but the various compounds have a wide range of potencies. As the bronchial tree is the major target organ for the carcinogenic effects of chromium(VI) compounds, and cancer primarily occurs following inhalation exposure, uptake in the respiratory organs is of great significance with respect to the cancer hazard and the subsequent risk of cancer in humans. IARC has stated that for chromium and certain chromium compounds there is sufficient evidence of carcinogenicity in humans (Group 1) *(1)*.

A large number of epidemiological studies have been carried out on the association between human exposure to chromates and the occurrence of cancer, particularly lung cancer, but only a few of these include measurements of exposure *(2–8)*. Measurements were made mainly at the time that the epidemiological studies were performed, whereas the carcinogenic effect is caused by exposure dating back 15–30 years. Hence, there is a great need for studies that include historical data on exposure.

Four sets of data for chromate production workers can be used for the quantitative risk assessment of chromium(VI) lifetime exposure *(3, 5–9)*. The average relative risk model is used in the following to estimate the incremental unit risk.

Using the study performed by Hayes et al. on chromium production workers *(3)*, several cohorts were investigated by Braver et al. *(8)* for cumulative exposure to chromium(VI) in terms of μg/m^3-years (cumulative exposure = usual exposure level in μg/m^3 × average duration of exposure). Average lifetime exposures for two cohorts can be calculated from the cumulative exposures of 670 and 3647 μg/m^3-years, as 2 μg/m^3 and 11.4 μg/m^3, respectively (X = μg/m^3 × 8/24 × 240/365 × (No. of years)/70).

The relative risk (RR) for these two cohorts, calculated from observed and expected cases of lung cancer, was 1.75 and 3.04. On the basis of the vital statistics data, the background lifetime probability of death due to lung cancer (P_0) is assumed to be 0.04. The risks (unit risk, UR) associated with a lifetime exposure to 1 μg/m^3 can therefore be calculated to be 1.5×10^{-2} and 7.2×10^{-3}, respectively ($UR = P_0(RR-1)/X$). The arithmetic mean of these two risk estimates is $1.1 \times l0^{-2}$.

A risk assessment can also be made on the basis of the study carried out by Langård et al. on ferrochromium plant workers in Norway *(5, 10)*. The chromium concentration to which the workers were exposed is not known, but measurements taken in 1975 showed a geometric mean value of about 530 μg/m^3. Assuming that the content of chromium(VI) in the sample was 19% and previous concentrations were at least as high as in 1975, the ambient concentration would have been about 100 μg/m^3. On the assumption that occupational exposure lasted for about 22 years, the average lifetime exposure can be determined as 6.9 μg/m^3 (X = 100 μg/m^3 × 8/24 × 240/365 × 22/70).

When workers in the same plant who were not exposed to chromium were used as a control population, the relative risk of lung cancer in chromium-exposed workers was calculated to be 8.5. The lifetime unit risk is therefore 4.3×10^{-2}.

Since earlier exposures must have been much higher than the values measured in 1975, the calculated unit risk of 4.3×10^{-2} can only be considered as an upper-bound estimate. The highest relative incidence ever demonstrated in chromate workers in Norway is about 38, at an exposure level for chromium(VI) of about 0.5 mg/m^3 *(6, 7)*. This relative rate is based on the incidence of bronchial cancer of 0.079 in the total Norwegian male population, irrespective of smoking status. If the average exposure duration is about 7 years, the average lifetime daily exposure is calculated to be 11 μg/m^3 (X = 500 μg/m^3 × 8/24 × 240/365 × 7/70). The incremental unit risk was calculated to be $1.3 \times l0^{-1}$. This very high lifetime risk may be due to the relatively small working population.

Differences in the epidemiological studies cited may suggest that the different hexavalent chromium compounds have varying degrees of carcinogenic potency.

The estimated lifetime risks based on various epidemiological data sets, in the range of 1.3×10^{-1} to $1.1 \times l0^{-2}$, are relatively consistent. As a best

estimate, the geometric mean of the risk estimates of 4×10^{-2} may be taken as the incremental unit risk resulting from a lifetime exposure to chromium(VI) at a concentration of 1 μg/m^3.

Using some other studies and different risk assessment models, the US Environmental Protection Agency (EPA) estimated the lifetime cancer risk due to exposure to chromium(VI) to be $1.2 \times l0^{-2}$. This estimate placed chromium(VI) in the first quartile of the 53 compounds evaluated by the EPA Carcinogen Assessment Group for relative carcinogenic potency *(11)*.

Guidelines

Information on the speciation of chromium in ambient air is essential since, when inhaled, only hexavalent chromium is carcinogenic in humans. The available data are derived from studies among chromium(VI)-exposed workers. When assuming a linear dose–response relationship between exposure to chromium(VI) compounds and lung cancer, no safe level of chromium(VI) can be recommended. At an air concentration of chromium(VI) of 1 μg/m^3, the lifetime risk is estimated to be 4×10^{-2}.

It should be noted that chromium concentration in air is often expressed as total chromium and not chromium(VI). The concentrations of chromium(VI) associated with an excess lifetime risk of 1:10 000, 1:100 000 and 1:1 000 000 are 2.5 ng/m^3, 0.25 ng/m^3 and 0.025 ng/m^3, respectively.

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6.5 Fluoride

Exposure evaluation

Exposure of the general European population to fluoride in its various chemical forms is highly variable. In heavily industrialized urban areas, typical daily inhalation intakes are in the range 10–40 µg/day (0.5–2 µg/m^3), and in some cases are as high as 60 µg/day (3 µg/m^3). Fluorides are emitted to the atmosphere in both gaseous and particulate forms, but studies typically only report total fluoride content.

The main sources of fluoride intake by humans are food and water. Except for occupational exposure, exposure to fluoride by inhalation is negligible.

Regarding occupational exposure, the daily amount of fluoride inhaled, assuming a total respiratory rate of 10 m^3 during a working day, could be 10–25 mg when the air concentration is at the most frequent exposure limits of 1–2.5 mg/m^3.

Health risk evaluation

The most important long-term adverse effect of fluorides on human populations is endemic skeletal fluorosis. The beneficial effect is prevention of caries, as a result both of fluoride incorporation into developing teeth and post-eruptive exposure of enamel to adequate levels of fluoride. It is therefore of crucial importance to gather information on fluoride sources in the diet, especially water, the etiology of early skeletal fluorosis as related to bone mineralization, and dose–response relationships *(1)*.

The earliest reports of skeletal fluorosis appeared from industries where exposure of workers to 100–500 µg/m^3 per 8-hour day for more than 4 years led to severe skeletal changes. Skeletal fluorosis has also been diagnosed in persons living in areas with excessive fluoride in soil, water, dust or plants *(1)*.

In one study, bronchial hyperreactivity was the main health effect at a mean fluoride concentration of 0.56 mg/m^3 and a mean particulate fluoride concentration of 0.15 mg/m^3 *(2)*. In a longitudinal study performed on 523 aluminium potroom workers, total fluoride was the most important risk factor among the exposure variables. In this study, the risk of developing asthmatic symptoms such as dyspnoea and wheezing was 3.4 and 5.2 times higher in the medium- and high-exposure groups, respectively,

than in the low-exposure group. Exposure to other pollutants was limited and did not appear to confound the results *(3)*.

Children living in the vicinity of a phosphate processing facility who were exposed to concentrations of about 100–500 μg/m^3 exhibited an impairment of respiratory function. It is not known, however, whether the concentrations were gaseous or total fluoride. In another study, no effects on respiratory function were observed at gaseous fluoride levels of up to 16 μg/m^3.

There is no evidence that atmospheric deposition of fluorides results in significant exposure through other routes, such as through contamination of soil and consequently groundwater.

Guidelines

For exposure of the general population to fluoride, reference exposure levels have been derived by applying a "benchmark dose" approach to a variety of animal and human exposure studies. The 1-hour reference exposure level to protect against any respiratory irritation is about 0.6 mg/m^3, and the level to protect against severe irritation from a once-in-a-lifetime release is about 1.6 mg/m^3 *(4)*.

Data from various sources indicate that prolonged exposure of humans (workers and children) to fluoride concentrations of 0.1–0.5 mg/m^3 leads to impairment of pulmonary function and skeletal fluorosis. No effects have been found at levels of up to 16 μg/m^3 gaseous fluoride. However, the available information does not permit the derivation of an air quality guideline value for fluoride(s).

Skeletal fluorosis is associated with a systemic uptake exceeding 5 mg/day in a relatively sensitive section of the general population. Systemic uptake from food and fluoridated water is about 3 mg/day. It is highly unlikely that ambient air concentrations of fluorides could pose any material risk of fluorosis.

It has been recognized that fluoride levels in ambient air should be less than 1 μg/m^3 to prevent effects on livestock and plants. These concentrations will also sufficiently protect human health.

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6.6 Hydrogen sulfide

Exposure evaluation

Typical symptoms and signs of hydrogen sulfide intoxication are most often caused by relatively high concentrations in occupational exposures. There are many occupations where there is a potential risk of hydrogen sulfide intoxication and, according to the US National Institute for Occupational Safety and Health *(1),* in the United States alone approximately 125 000 employees are potentially exposed to hydrogen sulfide. Low-level concentrations can occur more or less continuously in certain industries, such as in viscose rayon and pulp production, at oil refineries and in geothermal energy installations.

In geothermal areas there is a risk of exposure to hydrogen sulfide for the general population *(2).* The biodegradation of industrial wastes has been reported to cause ill effects in the general population *(2).* An accidental release of hydrogen sulfide into the air surrounding industrial facilities can cause very severe effects, as at Poza Rica, Mexico, where 320 people were hospitalized and 22 died *(2).* The occurrence of low-level concentrations of hydrogen sulfide around certain industrial installations is a well known fact.

Health risk evaluation

The first noticeable effect of hydrogen sulfide at low concentrations is its unpleasant odour. Conjunctival irritation is the next subjective symptom and can cause so-called "gas eye" at hydrogen sulfide concentrations of 70–140 mg/m^3. Table 16 shows the established dose–effect relationships for hydrogen sulfide.

The hazards caused by high concentrations of hydrogen sulfide are relatively well known, but information on human exposure to very low concentrations is scanty. Workers exposed to hydrogen sulfide concentrations of less than 30 mg/m^3 are reported to have rather diffuse neurological and mental symptoms *(4)* and to show no statistically significant differences when compared with a control group. On the other hand, changes in haem synthesis have been reported at hydrogen sulfide concentrations of less than 7.8 mg/m^3 (1.5–3 mg/m^3 average) *(5).* It is not known whether the inhibition is caused by the low concentrations or by the cumulative effects of occasional peak concentrations. Most probably, at concentrations below 1.5 mg/m^3 (1 ppm), even with exposure for longer periods, there are very few detectable health hazards in the toxicological sense. The malodorous

Table 16. Hydrogen sulfide: established dose–effect relationships

Hydrogen sulfide concentration		Effect	Reference
mg/m³	ppm		
1400–2800	1000–2000	Immediate collapse with paralysis of respiration	*(2)*
750–1400	530–1000	Strong central nervous system stimulation, hyperpnoea followed by respiratory arrest	*(2)*
450–750	320–530	Pulmonary oedema with risk of death	*(2)*
210–350	150–250	Loss of olfactory sense	*(3)*
70–140	50–100	Serious eye damage	*(3)*
15–30	10–20	Threshold for eye irritation	*(3)*

property of hydrogen sulfide is a source of annoyance for a large proportion of the general population at concentrations below 1.5 mg/m³, but from the existing data it cannot be concluded whether any health effects result. The need for epidemiological studies on possible effects of long-term, low-level hydrogen sulfide exposure is obvious. A satisfactory biological exposure indicator is also needed.

Guidelines

The LOAEL of hydrogen sulfide is 15 mg/m³, when eye irritation is caused. In view of the steep rise in the dose–effect curve implied by reports of serious eye damage at 70 mg/m³, an uncertainty factor of 100 is recommended, leading to a guideline value of 0.15 mg/m³ with an averaging time of 24 hours. A single report of changes in haem synthesis at a hydrogen sulfide concentration of 1.5 mg/m³ should be borne in mind.

In order to avoid substantial complaints about odour annoyance among the exposed population, hydrogen sulfide concentrations should not be allowed to exceed 7 µg/m³, with a 30-minute averaging period.

When setting concentration limits in ambient air, it should be remembered that in many places hydrogen sulfide is emitted from natural sources.

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6.7 Lead

Exposure evaluation

Average air lead levels are usually below 0.15 μg/m^3 at nonurban sites. Urban air lead levels are typically between 0.15 and 0.5 μg/m^3 in most European cities *(1–3)*. Additional routes of exposure must not be neglected, such as lead in dust, a cause of special concern for children.

The relationship between air lead exposure and blood lead has been shown to exhibit downward curvilinearity if the range of exposures is sufficiently large. At lower levels of exposure, the deviation from linearity is negligible and linear models of the relationship between intake and blood lead are satisfactory approximations.

The level of lead in blood is the best available indicator of current and recent past environmental exposure, and may also be a reasonably good indicator of lead body burden with stable exposures. Biological effects of lead will, therefore, be related to blood lead as an indicator of internal exposure.

Health risk evaluation

Table 17 summarizes LOAELs for haematological and neurological effects in adults. Cognitive effects in lead workers have not been observed at blood lead levels below 400 μg/l *(4, 5)*. Reductions in nerve conduction velocity were found in lead workers at blood levels as low as 300 μg/l *(6–8)*. Elevation of free erythrocyte protoporphyrin has been observed at blood levels of 200–300 μg/l. Delta-aminolaevulinic acid dehydrase (ALAD) inhibition is likely to occur at blood levels of about 100 μg/l *(9)*. Because of its uncertain biological significance relative to the functional reserve capacity of the haem biosynthetic system, ALAD inhibition is not treated as an adverse effect here.

Table 18 summarizes LOAELs for haematological, endocrinological and neurobehavioural endpoints in children. Reduced haemoglobin levels have been found at concentrations in blood of around 400 μg/l. Haematocrit values below 35% have not been reported at blood levels below 200 μg/l *(10)*; this is also true for several enzyme systems, which may be of clinical significance.

Central nervous system effects, as assessed by neurobehavioural endpoints, appear to occur at levels below 200 μg/l. Consistent effects have been

Table 17. Summary of LOAELs for lead-induced health effects in adults

LOAEL at given blood lead level (µg/l)	Haem synthesis, haematological and other effects	Effects on the nervous system
1000–1200		Encephalopathic signs and symptoms
800	Frank anaemia	
500	Reduced haemoglobin production	Overt subencephalopathic neurological symptoms, cognition impairment
400	Increased urinary ALA and elevated coproporphyrin	
300		Peripheral nerve dysfunction (slowed nerve conduction velocities)
200–300	Erythrocyte protoporphyrin elevation in males	
150–200	Erythrocyte protoporphyrin elevation in females	

Table 18. Summary of LOAELs for lead-induced health effects in children

LOAEL at given blood lead level (µg/l)	Haem synthesis, haematological and other effects	Effects on the nervous system
800–1000		Encephalopathic signs and symptoms
700	Frank anaemia	
400	Increased urinary delta-aminolaevulinic acid and elevated coproporphyrin	
250–300	Reduced haemoglobin synthesis	
150–200	Erythrocyte protoporphyrin elevation	
100–150	Vitamin D3 reduction	Cognitive impairment
100	ALAD inhibition	Hearing impairment

reported for global measures of cognitive functioning, such as the psychometric IQ, to be associated with blood lead levels of 100–150 µg/l *(11, 12)*. Some epidemiological studies have indicated effects at blood lead levels below 100 µg/l. Existing animal studies do provide qualitative support for the claim of lead as the causative agent *(12)*.

Guidelines

Guidelines for lead in air will be based on the concentration of lead in blood. Critical effects to be considered in the adult organism include elevation of free erythrocyte protoporphyrin, whereas for children cognitive deficit, hearing impairment and disturbed vitamin D metabolism *(13, 14)* are taken as the decisive effects. All of these effects are considered adverse. A critical level of lead in blood of 100 µg/l is proposed. It should be stressed that all of these values are based on population studies yielding group averages, which apply to the individual child only in a probabilistic manner. Although some lead salts have been found to be carcinogenic in animals, the evidence for a carcinogenic potential in humans is inadequate and will, therefore, not be considered here.

For the derivation of a guideline value, the following arguments have been considered.

- Currently measured "baseline" blood lead levels of minimal anthropogenic origin are probably in the range10–30 µg/l.

- Various international expert groups have determined that the earliest adverse effects of lead in populations of young children begin at 100–150 µg/l. Although it cannot be excluded that population effects may occur below this range, it is assumed to be prudent to derive a guideline value based on the lowest value in this range (100 µg/l).

- It can be assumed that inhalation of airborne lead is a significant route of exposure for adults (including pregnant women) but is of less significance for young children, for whom other pathways of exposure such as ingested lead are generally more important.

- It appears that 1 µg lead per m^3 air directly contributes approximately 19 µg lead per litre blood in children and about 16 µg per litre blood in adults, although it is accepted that the relative contribution from air is less significant in children than in adults. These values are approximations, recognizing that the relationships are curvilinear in nature and will apply principally at lower blood lead levels.

- It must be taken into account that, in typical situations, an increase of lead in air also contributes to increased lead uptake by indirect environmental pathways. To correct for uptake by other routes as well, it is assumed that 1 µg lead per m^3 air would contribute to 50 µg lead per litre blood.

- It is recommended that efforts be made to ensure that at least 98% of an exposed population, including preschool children, have blood lead levels that do not exceed 100 µg/l. In this case, the median blood lead level would not exceed 54 µg/l. On this basis, the annual average lead level in air should not exceed 0.5 µg/m^3. This proposal is based on the assumption that the upper limit of nonanthropogenic blood is 30 µg/l. These estimates are assumed to protect adults also.

- To prevent further increases of lead in soils and consequent increases in the exposure of future generations, air lead levels should be kept as low as possible.

Since both direct and indirect exposure of young children to lead in air occurs, the air guidelines for lead should be accompanied by other preventive measures. These should specifically take the form of monitoring the lead content of dust and soils arising from lead fallout. The normal hand-to-mouth behaviour of children with regard to dust and soil defines these media as potentially serious sources of exposure. A specific monitoring value is not recommended. Some data indicate that lead fallout in excess of 250 µg/m^2 per day will increase blood lead levels.

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6.8 Manganese

Exposure evaluation

In urban and rural areas without significant manganese pollution, annual averages are mainly in the range of 0.01–0.07 μg/m^3; near foundries the level can rise to an annual average of 0.2–0.3 μg/m^3 and, where ferro- and silico-manganese industries are present, to more than 0.5 μg/m^3, with individual 24-hour concentrations sometimes exceeding 10 μg/m^3 *(1, 2)*.

Health risk evaluation

The toxicity of manganese varies according to the route of exposure. By ingestion, manganese has relatively low toxicity at typical exposure levels and is considered a nutritionally essential trace element. By inhalation, however, manganese has been known since the early nineteenth century to be toxic to workers. Manganism is characterized by various psychiatric and movement disorders, with some general resemblance to Parkinson's disease in terms of difficulties in the fine control of some movements, lack of facial expression, and involvement of underlying neuroanatomical (extrapyramidal) and neurochemical (dopaminergic) systems *(3–5)*. Respiratory effects such as pneumonitis and pneumonia and reproductive dysfunction such as reduced libido are also frequently reported features of occupational manganese intoxication. The available evidence is inadequate to determine whether or not manganese is carcinogenic; some reports suggest that it may even be protective against cancer. Based on this mixed but insufficient evidence, the US Environmental Protection Agency has concluded that manganese is not classifiable as to human carcinogenicity *(6)*. IARC has not evaluated manganese *(7)*.

Several epidemiological studies of workers have provided consistent evidence of neurotoxicity associated with low-level manganese exposure. Sufficient information was available to develop a benchmark dose using the study by Roels et al. *(3)*, thereby obviating the need to account for a LOAEL to NOAEL extrapolation. With regard to exposure, both lifetime integrated respirable dust concentrations as well as current respirable dust concentrations were considered. Correlation between effects and exposure was strongest for eye–hand coordination with current concentration of respirable dust. From the data of Roels et al. *(3)*, lower 95% confidence limits of the best concentration estimate giving respectively a 10% effect ($BMDL_{10}$) of 74 μg/m^3 and a 5% effect ($BMDL_5$) of 30 μg/m^3 were calculated *(8)*. Taking a conservative approach, the lower 95% confidence limit of the $BMDL_5$ values was chosen as representative of the NOAEL.

$BMDL_5$ values for the other exposure measures (time-integrated and average concentration of respirable dust) are not substantially different *(5)*.

In evaluating the potential health risks associated with inhalation exposure to manganese, various uncertainties must be taken into consideration. Virtually all of the human health evidence is based on healthy, adult male workers; other, possibly more sensitive populations have not been adequately investigated. Also, the potential reproductive and developmental toxicity of inhaled manganese has not been fully investigated.

Guidelines

Based on neurotoxic effects observed in occupationally exposed workers and using the benchmark approach, an estimated NOAEL (the lower 95% confidence limit of the $BMDL_5$) of 30 μg/m^3 was obtained. A guideline value for manganese of 0.15 μg/m^3 was derived by dividing by a factor of 4.2 to adjust for continuous exposure and an uncertainty factor of 50 (10 for interindividual variation and 5 for developmental effects in younger children). This latter factor was chosen by analogy with lead where neurobehavioural effects were found in younger children at blood lead levels five times lower than in adults and supported by evidence from studies of experimental animals. The adjustment for continuous exposure was considered sufficient to account for long-term exposure based on knowledge of the half-time of manganese in the brain. The guideline value should be applied as an annual average.

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6.9 Mercury

Exposure evaluation

In areas remote from industry, atmospheric levels of mercury are about 2–4 ng/m^3, and in urban areas about 10 ng/m^3. This means that the daily amount absorbed into the bloodstream from the atmosphere as a result of respiratory exposure is about 32–64 ng in remote areas, and about 160 ng in urban areas. However, this exposure to mercury from outdoor air is marginal compared to exposure from dental amalgams, given that the estimated average daily absorption of mercury vapour from dental fillings varies between 3000 and 17 000 ng.

Health risk evaluation

Sensitive population groups

With regard to exposure to mercury vapour, sensitive population groups have not been conclusively identified from epidemiological, clinical or experimental studies. Nevertheless, the genetic expression of the enzyme catalase, which catalyses the oxidation of mercury vapour to divalent mercuric ion, varies throughout populations. Swiss and Swedish studies have revealed a gene frequency of the order of 0.006 for this trait *(1, 2)*. Thus 30–40 per million of the population are almost completely lacking catalase activity (homozygotes) and 1.2% are heterozygotes with a 60% reduction in catalase activity. Information is lacking on the degree to which other enzymes in the blood are able to take over the oxidation.

Effects on the kidney of inorganic mercury and phenylmercury are believed to occur first in a subgroup of individuals whose susceptibility may be genetically determined, although the proportion of this subgroup in the general population is unknown. Virtually nothing is known about the relative sensitivity at different stages of the life cycle to mercury vapour or inorganic cationic compounds, except that the developing rat kidney is less sensitive than the mature tissue to inorganic mercury *(3)*.

The prenatal stage appears to be the period of life when sensitivity to methylmercury is at its greatest; neuromotor effects in exposed Iraqi populations indicated that sensitivity at this time is at least three times greater than that in adults *(4)*.

Mercury vapour

Time-weighted air concentrations are the usual means of assessing human exposure. Reported air values depend on the type of sampling. Static sampling generally gives lower values than personal sampling. In order to convert the air concentrations quoted in Table 19 to equivalent concentrations in ambient air, two factors have to be taken into account. First, the air concentrations listed in Table 19 were measured in the working environment using static samplers. The conversion factor may vary, depending on exposure conditions. The values shown should be increased by a factor of 3 to correspond to the true air concentrations inhaled by the workers as determined by personal samplers. Second, the total amount of air inhaled at the workplace per week is assumed to be 50 m^3 (10 m^3/day × 5 days) whereas the amount of ambient air inhaled per week would be 140 m^3 (20 m^3/day × 7 days). Thus the volume of ambient air inhaled per week is approximately three times the volume inhaled at the workplace. Thus, to convert the workplace air concentrations quoted in Table 19 to equivalent ambient air concentrations, they should first be multiplied by 3 to convert to actual concentrations in the workplace, and divided by 3 to correct for the greater amount of ambient air inhaled per week by the average adult. It follows that the mercury vapour concentrations quoted in Table 19 are approximately equivalent to ambient air concentrations.

Table 19. Concentrations of total mercury in air and urine at which effects are observed at a low frequency in workers subjected to long-term exposure to mercury vapour

Observed effect [a]	Mercury level		Reference
	Air [b] (µg/m^3)	Urine (µg/litre)	
Objective tremor	30	100	*(5)*
Renal tubular effects; changes in plasma enzymes	15 [c]	50	*(6)*
Nonspecific symptoms	10–30	25–100	*(5)*

[a] These effects occur with low frequency in occupationally exposed groups. Other effects have been reported, but air and urine levels are not available.

[b] The air concentrations measured by static air samplers are taken as a time-weighted average, assuming 40 hours per week for long-term exposure (at least five biological half-times, equivalent to 250 days).

[c] Calculated from the urine concentration, assuming that a mercury concentration in air of 100 µg/m^3 measured by static samplers is equivalent to a mercury concentration of 300 µg/litre in the urine.

Since these figures are based on observations in humans, an uncertainty factor of 10 would seem appropriate. However, the LOAELs in Table 19 are rough estimates of air concentrations at which effects occur at a "low frequency". Because it seems unlikely that such effects would occur in occupationally exposed workers at air concentrations as low as one half of those given in Table 19, it seems appropriate to use an uncertainty factor of 20. Thus, the estimated guideline for mercury concentration in air would be 1 μg/m^3.

Inorganic compounds

Cationic forms of inorganic mercury are retained in the lungs about half as efficiently as inhaled mercury vapour (40% versus 80% retained); thus the estimated guideline providing adequate protection against renal tubular effects would be twice as high as that for mercury vapour.

Methylmercury compounds

It does not seem appropriate to set air quality guidelines for methylmercury compounds. Inhalation of this form of mercury, if it is present in the atmosphere, would make a negligible contribution to total human intake. Nevertheless, mercury in the atmosphere may ultimately be converted to methylmercury following deposition on soils or sediments in natural bodies of water, leading to an accumulation of that form of mercury in aquatic food chains. In this situation, guidelines for food intake would be appropriate, such as those recommended by the Joint FAO/WHO Expert Committee on Food Additives.

Guidelines

It is necessary to take into account the different forms of mercury in the atmosphere and the intake of these forms of mercury from other media. The atmosphere and dental amalgam are the sole sources of exposure to mercury vapour, whereas the diet is the dominant source of methylmercury compounds.

Current levels of mercury in outdoor air, except for regional "hot spots", are typically in the order of 0.005–0.010 μg/m^3 and thus are marginal compared to exposure from dental amalgam. The exposure to mercury from outdoor air at these air levels is not expected to have direct effects on human health.

The predominant species of mercury present in air, Hg^0, is neither mutagenic nor carcinogenic. Exposure to airborne methylmercury is 2–3 orders of magnitude below the food-related daily intake and will, in this context,

be regarded as insignificant. It is thus only possible to derive a numerical guideline for inhalation of inorganic mercury, by including mercury vapour and divalent mercury.

The LOAELs for mercury vapour are around 15–30 μg/m^3. Applying an uncertainty factor of 20 (10 for uncertainty due to variable sensitivities in higher risk populations and, on the basis of dose–response information, a factor of 2 to extrapolate from a LOAEL to a likely NOAEL), a guideline for inorganic mercury vapour of 1 μg/m^3 as an annual average has been established. Since cationic inorganic mercury is retained only half as much as the vapour, the guideline also protects against mild renal effects caused by cationic inorganic mercury. Present knowledge suggests, however, that effects on the immune system at lower exposures cannot be excluded.

An increase in ambient air levels of mercury will result in an increase in deposition in natural bodies of water, possibly leading to elevated concentrations of methylmercury in freshwater fish. Such a contingency might have an important bearing on acceptable levels of mercury in the atmosphere. Unfortunately, the limited knowledge of the global cycle and of the methylation and bioaccumulation pathways in the aquatic food chain does not allow any quantitative estimates of risks from these post-depositional processes. Therefore, an ambient air quality guideline value that would fully prevent the potential for adverse health impacts of post-depositional methylmercury formation cannot be proposed. To prevent possible health effects in the near future, however, ambient air levels of mercury should be kept as low as possible.

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6.10 Nickel

Exposure evaluation

Nickel is present throughout nature and is released into air and water both from natural sources and as a result of human activity.

In nonsmokers, about 99% of the estimated daily nickel absorption stems from food and water; for smokers the figure is about 75%. Nickel levels in the ambient air are in the range 1–10 ng/m^3 in urban areas, although much higher levels (110–180 ng/m^3) have been recorded in heavily industrialized areas and larger cities. There is, however, limited information on the species of nickel in ambient air.

Consumer products made from nickel alloys and nickel-plated items lead to cutaneous contact exposure.

Exposure to nickel levels of 10–100 mg/m^3 have been recorded for occupational groups, with documented increased cancer risk. Exposure levels in the refining industry are currently usually less than 1–2 mg/m^3, often less than 0.5 mg/m^3. Experimental and epidemiological data indicate that the nickel species in question is important for risk estimation.

Health risk evaluation

Allergic skin reactions are the most common health effect of nickel, affecting about 2% of the male and 11% of the female population. Nickel content in consumer products and possibly in food and water are critical for the dermatological effect. The respiratory tract is also a target organ for allergic manifestations of occupational nickel exposure.

Work-related exposure in the nickel-refining industry has been documented to cause an increased risk of lung and nasal cancers. Inhalation of a mixture of oxidic, sulfidic and soluble nickel compounds at concentrations higher than 0.5 mg/m^3, often considerably higher, for many years has been reported *(1)*.

Nickel has a strong and prevalent allergenic potency. There is no evidence that airborne nickel causes allergic reactions in the general population, although this reaction is well documented in the working environment. The key criterion for assessing the risk of nickel exposure is its carcinogenic potential.

In general, nickel compounds give negative results in short-term bacterial mutagenicity tests because of limited uptake. Nevertheless, they show a wide range of transformation potencies in mammalian cell assays, depending mainly on their bioavailability.

Both green nickel oxide and the subsulfide have caused tumours in animal inhalation studies. In addition, nickel monoxide (not further specified) and an alloy with 66.5% nickel and 12.5% chromium caused tumours following tracheal instillation. A corresponding instillation with an alloy of 26.8% nickel and 16.2% chromium had no such effect, indicating that it was nickel and not chromium that caused the tumours. Injection-site tumours in a number of organs are found with many particulate nickel compounds. The tumorigenic potency varies with chemical composition, solubility and particle surface properties *(2, 3)*.

Epidemiological evidence from the nickel-refining industry indicates that sulfidic, oxidic and soluble nickel compounds are all carcinogenic. Exposure to metallic nickel has not been demonstrated to cause cancer in workers.

Several theories have been suggested for the mechanisms of nickel tumorigenesis. All of these assume that the nickel ion is the ultimate active agent. On the basis of the underlying concept that all nickel compounds can generate nickel ions that are transported to critical sites in target cells, IARC has classified nickel compounds as carcinogenic to humans (Group 1) and metallic nickel as possibly carcinogenic to humans (Group 2B) *(4)*.

On the basis of one inhalation study *(5)*, the US Environmental Protection Agency (EPA) classified nickel subsulfide as a class A carcinogen and estimated the maximum likelihood incremental unit risk to be $1.8–4.1 \times 10^{-3}$ *(6)*. This study, however, involves only exposure to nickel subsulfide. It is not known whether this compound is present in ambient air, but since it is probably one of the most potent nickel compounds, this risk estimate may represent an upper limit, if accepted. WHO estimated an incremental unit risk of 4×10^{-4} per $\mu g/m^3$ calculated from epidemiological results *(7)*.

On the basis of epidemiological studies, EPA classified nickel dust as a class A carcinogen and estimated the lifetime cancer risk from exposure to nickel dust to be 2.4×10^{-4}. This estimate placed nickel in the third quartile of the 55 substances evaluated by the EPA Carcinogen Assessment Group with regard to their relative carcinogenic potency *(8)*. Assuming a content of 50% of nickel subsulfide in total dust, a unit risk of 4.8×10^{-4} was estimated for this compound.

An estimate of unit risk can be given on the basis of the report of lung cancer in workers first employed between 1968 and 1972 and followed through to 1987 in Norway *(9, 10)*. Using the estimated risk of 1.9 for this group and an exposure of 2.5 mg/m^3, a lifetime exposure of 155 µg/m^3 and a unit risk of 3.8×10^{-4} per µg/m^3 can be calculated.

Guidelines

Even if the dermatological effects of nickel are the most common, such effects are not considered to be critically linked to ambient air levels.

Nickel compounds are human carcinogens by inhalation exposure. The present data are derived from studies in occupationally exposed human populations. Assuming a linear dose–response, no safe level for nickel compounds can be recommended.

On the basis of the most recent information of exposure and risk estimated in industrial populations, an incremental risk of 3.8×10^{-4} can be given for a concentration of nickel in air of 1 µg/m^3. The concentrations corresponding to an excess lifetime risk of 1:10 000, 1:100 000 and 1: 1 000 000 are about 250, 25 and 2.5 ng/m^3, respectively.

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6.11 Platinum

Exposure evaluation

There is currently very little information on levels of exposure to soluble platinum compounds in the general environment, and there are no authenticated observations on adverse health effects in the population resulting from such exposure. The available data derived from air sampling and from dust deposition of total platinum are limited. Ambient air concentrations of platinum compounds that would occur in different scenarios have been estimated using dispersion models developed by the US Environmental Protection Agency *(1)*. Ambient air concentrations of total platinum in various urban exposure situations, assuming an average emission rate of approximately 20 ng/km from the monolithic three-way catalyst, were estimated. These concentrations are lower by a factor of 100 than those estimated for the old, pellet-type catalyst. In the exposure conditions studied, estimated ambient air concentrations of platinum ranged from 0.05 pg/m^3 to 0.09 ng/m^3. The WHO Task Group on Environmental Health Criteria for Platinum considered that environmental contamination with platinum from the monolithic three-way catalyst is likely to be very low or negligible *(2)*. The Group concluded that platinum-containing exhaust emissions from such catalysts most probably do not pose a risk for adverse health effects in the general population but it was recommended that, to be on the safe side, the possibility should be kept under review.

A recently completed pilot study sought to acquire information on direct and indirect sources and emissions of platinum group metals in the United Kingdom environment *(3)*. With regard to emissions from motor vehicle catalytic converters, samples of road dusts and soils were collected from areas with high and low traffic flows, for platinum and lead estimation. Higher levels of platinum were found in dusts and soils at major road intersections and on roads with high traffic densities, indicating traffic as the source of platinum at these sites *(4)*.

As platinum in road dust is at least partially soluble, it may enter the food chain so that diet may also be a major source of platinum intake in the non-industrially exposed population. This is suggested by the total diet study carried out in Australia in Sydney, an area of high traffic density, and Lord Howe Island, an area with very low traffic density. Blood platinum levels were similar in the two locations *(5)*.

In early studies on platinum-exposed workers, exposure levels were high. Values ranged from 0.9 to 1700 μg/m^3 in four British platinum refineries, giving rise to symptoms in 57% of the exposed workers *(6)*. Following the adoption of an occupational exposure limit with a threshold limit value (TLV) for soluble platinum salts of 2 μg/m^3 as an 8-hour time-weighted average, the incidence of platinum salt hypersensitivity has fallen, but sensitization in workers has still been observed. Thus, in a cross-sectional survey, skin sensitization was reported in 19% of 65 workers in a platinum refinery, where analysis of airborne dust showed levels of soluble platinum of 0.08–0.1 μg/m^3 in one department and less than 0.05 μg/m^3 in other areas *(7)*. In another plant with air levels generally below 0.08 μg/m^3, 20% of exposed workers were sensitized *(8)*. It is possible, however, that short, sharp exposures to concentrations above the TLV could have been responsible for some of these effects. In a 4-month study in a United States platinum refinery with a high prevalence of rhinitis and asthma, workplace concentrations exceeded the occupational limit of 2 μg/m^3 for 50–75% of the time *(9)*. The risk of developing platinum salt sensitivity appears to be correlated with exposure intensity, the highest incidence occurring in groups with the highest exposure, although no unequivocal concentration–effect relationship can be deduced from the reported studies.

Health risk evaluation

There is no convincing evidence for sensitization or for other adverse health effects following exposure to metallic platinum. Exposure to the halogenated platinum complexes already described has given rise to sensitization following occupational exposure to platinum concentrations in air greater than the TLV of 2 μg/m^3, and may have caused sensitization reactions at concentrations down to and even below the limit of detection in workplace monitoring of 0.05 μg/m^3. Furthermore, as subsequent exposure to minute concentrations of these platinum salts may lead to a recurrence of the health effects shown in Table 20 in previously sensitized subjects, it is not possible to define a no-effect level for these platinum compounds.

Because the correlation between platinum exposure concentration and the development of sensitization is unknown, the WHO Task Group *(2)* considered that a recommendation for a reduction in the occupational exposure limit cannot at present be justified. It did, however, recommend that the occupational exposure limit of 2 μg/m^3 be changed from an 8-hour time-weighted average to a ceiling value, and that personal sampling devices be used in conjunction with area sampling to determine more correctly the true platinum exposure. Should it be ascertained unequivocally that sensitization has occurred in workers consistently exposed to platinum

Table 20. Concentration–effect data for platinum

Concentration range	Average duration of exposure	Frequency of health effects in the general population	Health effects in susceptible groups
Airborne dust level for soluble platinum salts above the TLV time-weighted average of 2 μg/m^3	Varies from weeks to years	No data available	In some occupationally exposed individuals: conjunctivitis, rhinitis, cough, wheeze, dyspnoea, asthma, contact dermatitis, urticaria, mucous membrane inflammation
Airborne dust level for soluble platinum salts < 0.05 μg/m^3			Possibility that the above effects cannot be excluded Recurrence of the above effects in subjects previously sensitized Conversion to positive skin-prick test

levels below the current exposure limit of 2 μg/m^3, and that intermittent, short exposures above this level had not taken place, there would be strong grounds for reducing the exposure limit.

The degree of solubilization and perhaps conversion to halide complexes of platinum particulate matter emitted into the general environment is not known, but is likely to be small. The prevalence of asthma in industrialized communities is increasing markedly. While there are no observations to suggest that platinum (emitted from vehicle catalytic converters or from industrial sources, deposited and in part converted in the general environment into halide salts) may act as an etiological agent, it would be inappropriate in the present state of knowledge to propose a no-effect level. From observations following occupational exposure, a value of 0.05 μg/m^3 for soluble platinum salts may be considered as a tentative LOAEL. Platinum levels in air in the general environment are at least three orders of magnitude below this figure.

While *cis*-platin, an IARC Group 2A carcinogen, is released into the environment following medical use, there are no grounds for considering this platinum compound or its analogues as significant atmospheric pollutants.

Guidelines

In occupational settings, sensitization reactions have been observed for soluble platinum down to the limit of detection of 0.05 µg/m^3. However, these effects have occurred only in individuals previously sensitized by higher exposure levels. It is unlikely that the general population exposed to ambient concentrations of soluble platinum, which are at least three orders of magnitude lower, will develop similar effects. At present no specific guideline value is recommended but further studies are required, in particular on the speciation of platinum in the environment.

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6.12 Vanadium

Exposure evaluation

The natural background level of vanadium in air in Canada has been reported to be in the range 0.02–1.9 ng/m^3 *(1)*. Vanadium concentrations recorded in rural areas varied from a few nanograms to tenths of a nanogram per m^3, and in urban areas from 50 ng/m^3 to 200 ng/m^3. In cities during the winter, when fuel oil with a high vanadium content was used for heating, concentrations as high as 2000 ng/m^3 were reported. Air pollution by industrial plants may be less than that caused by power stations and heating equipment.

The concentrations of vanadium in workplace air (0.01–60 mg/m^3) are much higher than those in the general environment.

Health risk evaluation

The acute and chronic effects of vanadium exposure on the respiratory system of occupationally exposed workers should be regarded as the most significant factors when establishing air quality guidelines. Most of the clinical symptoms reported reflect irritative effects of vanadium on the upper respiratory tract, except at higher concentrations (above 1 mg vanadium per m^3), when more serious effects on the lower respiratory tract are observed. Clinical symptoms of acute exposure are reported *(2)* in workers exposed to concentrations ranging from 80 µg to several mg vanadium per m^3, and in healthy volunteers *(3)* exposed to concentrations of 56–560 µg/m^3 (Table 21).

A study of occupationally exposed groups provides data reasonably consistent with those obtained from controlled acute human exposure experiments, suggesting that the LOAEL for acute exposure can be considered to be 60 µg/m^3.

Chronic exposure to vanadium compounds revealed a continuum in the respiratory effects, ranging from slight changes in the upper respiratory tract, with irritation, coughing and injection of pharynx, detectable at 20 µg/m^3, to more serious effects such as chronic bronchitis and pneumonitis, which occurred at levels above 1 mg/m^3. Occupational studies illustrate the concentration–effect relationship at low levels of exposure *(4–6)*, showing increased prevalence of irritative symptoms of the upper respiratory tract; this suggests that 20 µg/m^3 can be regarded as the LOAEL for

Table 21. Respiratory effects after acute and chronic exposures to low levels of vanadium

Type of exposure	Vanadium compound	Concentration in µg/m^3		Symptoms	Reference
		Compound	Vanadium		
Acute					
Boiler cleaning	V_2O_5 V_2O_3	523	80	Changes in parameters of lung functions	*(2)*
Clinical study (experimental 8-hour exposure)	V_2O_5	1000	560	Respiratory irritation: persistent and frequent cough, expiratory wheezes	*(3)*
	V_2O_5	200	112	Persistent cough (7- 1 0 days)	
	V_2O_5	100	56	Slight cough for 4 days	
Chronic					
Vanadium refinery	V_2O_5	536	300	Respiratory irritation: cough, sputum, nose and throat irritation, injected pharynx	*(4)*
Vanadium refinery	V_2O_5	18-71	10-40	Irritative changes of mucous membranes of upper respiratory tract	*(5)*
Vanadium processing	V_2O_5 V_2O_3	—	1.2-12.0	Respiratory irritation: injected pharynx	*(6)*

chronic exposure (Table 21). There are no conclusive data on the health effects of exposure to airborne vanadium at present concentrations in the general population, and a susceptible subpopulation is not known. Vanadium is a potent respiratory irritant, however, which would suggest that asthmatics should be considered a special group at risk.

There are no well documented animal data to support findings in human studies, although one study reported systemic and local respiratory effects in rats at levels of 3.4–l5 μg/m^3 *(7)*.

Guidelines

Available data from occupational studies suggest that the LOAEL of vanadium can be assumed to be 20 μg/m^3, based on chronic upper respiratory tract symptoms. Since the adverse nature of the observed effects on the upper respiratory tract were minimal at this concentration, and a susceptible subpopulation has not been identified, a protection factor of 20 was selected. It is believed that below 1 μg/m^3 (averaging time 24 hours) environmental exposure to vanadium is not likely to have adverse effects on health.

The available evidence indicates that the current vanadium levels generally found in industrialized countries are not in the range associated with potentially harmful effects.

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CHAPTER 7

Classical pollutants

7.1 Nitrogen dioxide

Exposure evaluation

Levels of nitrogen dioxide vary widely because a continuous baseline level is frequently present, with peaks of higher levels superimposed. Natural background annual mean concentrations are in the range 0.4–9.4 μg/m^3. Outdoor urban levels have an annual mean range of 20–90 μg/m^3 and hourly maxima in the range 75–1015 μg/m^3. Levels indoors where there are unvented gas combustion appliances may average more than 200 μg/m^3 over a period of several days. A maximum 1-hour peak may reach 2000 μg/m^3. For briefer periods, even higher concentrations have been measured.

Critical concentration–response data

Monotonic concentration–response data are available only from a few animal studies. Thus, this section will focus on lowest-observed-effect levels and their interpretation.

Short-term exposure effects

Available data from animal toxicology experiments rarely indicate the effects of acute exposure to nitrogen dioxide concentrations of less than 1880 μg/m^3 (1 ppm). Normal healthy people exposed at rest or with light exercise for less than 2 hours to concentrations of more than 4700 μg/m^3 (2.5 ppm) experience pronounced decrements in pulmonary function; generally, such people are not affected at less than 1880 μg/m^3 (1 ppm). One study showed that the lung function of people with chronic obstructive pulmonary disease is slightly affected by a 3.75-hour exposure to 560 μg/m^3 (0.3 ppm) *(1)*. A wide range of findings in asthmatics has been reported; one study observed no effects from a 75-minute exposure to 7520 μg/m^3 (4 ppm) *(2)*, whereas others showed decreases in FEV_1 after 10 minutes of exercise during exposure to 560 μg/m^3 (0.3 ppm) *(3)*.

Asthmatics are likely to be the most sensitive subjects, although uncertainties exist in the health database. The lowest concentration causing effects on pulmonary function was reported from two laboratories that exposed mild asthmatics for 30–110 minutes to 560 μg/m^3 (0.3 ppm) during intermittent exercise. However, neither of these laboratories was able to replicate these responses with a larger group of asthmatic subjects. One of these studies indicated that nitrogen dioxide can increase airway reactivity to cold air in asthmatics. At lower concentrations, the pulmonary function of asthmatics was not changed significantly.

Nitrogen dioxide increases bronchial reactivity as measured by pharmacological bronchoconstrictor agents in normal and asthmatic subjects, even at levels that do not affect pulmonary function directly in the absence of a bronchoconstrictor. Asthmatics appear to be more susceptible. For example, some but not all studies show increased responsiveness to bronchoconstrictors at nitrogen dioxide levels as low as 376–560 μg/m^3 (0.2–0.3 ppm); in other studies, higher levels had no such effect. Because the actual mechanisms are not fully defined and nitrogen dioxide studies with allergen challenges showed no effects at the lowest concentration tested (190 μg/m^3; 0.1 ppm), full evaluation of the health consequences of the increased responsiveness to bronchoconstrictors is not yet possible.

Long-term exposure effects

Studies with animals have clearly shown that several weeks to months of exposure to nitrogen dioxide concentrations of less than 1880 μg/m^3 (1 ppm) cause a plethora of effects, primarily in the lung but also in other organs, such as the spleen, liver and blood. Both reversible and irreversible lung effects have been observed. Structural changes range from a change in cell types in the tracheobronchial and pulmonary regions (lowest reported level 640 μg/m^3) to emphysema-like effects (at concentrations much higher than ambient). Biochemical changes often reflect cellular alterations (lowest reported levels for several studies 380–750 μg/m^3 (0.2–0.4 ppm) but isolated cases at lower effective concentrations). Nitrogen dioxide levels as low as 940 μg/m^3 (0.5 ppm) also increase susceptibility to bacterial and viral infection of the lung *(4)*.

There are no epidemiological studies that can be confidently used quantitatively to estimate long-term nitrogen dioxide exposure durations or concentrations likely to be associated with the induction of unacceptable health risks in children or adults. Because homes with gas cooking appliances have peak nitrogen dioxide levels that are in the same range as levels causing effects in some animal and human clinical studies, epidemiological studies evaluating the effects of nitrogen dioxide exposures in such homes have been of much interest. In general, epidemiological studies on adults and on infants under 2 years showed no significant effect of the use of gas cooking appliances on respiratory illness; nor do the few available studies of infants and adults show any associations between pulmonary function changes and gas stove use. However, children aged 5–12 years are estimated to have a 20% increased risk for respiratory symptoms and disease for each increase in nitrogen dioxide concentration of 28.3 μg/m^3 (2-week average) where the weekly average concentrations are in the range 15–128 μg/m^3 or possibly higher. Nevertheless, the observed effects cannot clearly be attributed to

either the repeated short-term high-level peak exposures or long-term exposures in the range of the stated weekly averages (or possibly both).

As hinted at by the indoor studies, the results of outdoor studies tend to point consistently toward increased respiratory symptoms, their duration, and/or lung function decrements being qualitatively associated in children with long-term ambient nitrogen dioxide exposures. Outdoor epidemiology studies, as with indoor studies, however, provide little evidence for the association of long-term ambient exposures with health effects in adults. None of the available studies yields confident estimates of long-term exposure–effect levels, but available results are most clearly suggestive of respiratory effects in children at annual average nitrogen dioxide concentrations of 50–75 μg/m^3 or higher.

Health risk evaluation

Small, statistically significant, reversible effects on lung function and airway responsiveness have been observed in mild asthmatics during a 30-minute exposure to nitrogen dioxide concentrations of 380–560 μg/m^3 (0.2–0.3 ppm). The sequelae of repetitive exposures of such individuals or the impact of single exposures on more severe asthmatics are not known. In most animal experiments, however, 1–6 months of exposure to 560–940 μg/m^3 are required to produce changes in lung structure, lung metabolism and lung defences against bacterial infection. Thus, it is prudent to avoid exposures in humans, because repetitive exposures in animals lead to adverse effects. Animal toxicology studies of lung host defence and morphology suggest that peak concentrations contribute more to the toxicity of nitrogen dioxide than does duration, although duration is still important. Nitrogen dioxide puts children at increased risk of respiratory illness. This is of concern because repeated lung infections in children can cause lung damage later in life.

Nitrogen dioxide presents a dilemma with respect to guidelines. It is clear that the public should be protected from excessive exposure, but the recommendation of a guideline is complicated owing to the difficulties posed by the uncertainties in exposure–response relationships for both acute (< 3-hour) and long-term exposure, and the uncertainties in establishing an appropriate margin of protection. Studies of asthmatics exposed to 380–560 μg/m^3 indicate a change of about 5% in pulmonary function and an increase in airway responsiveness to bronchoconstrictors. Asthmatics are more susceptible to the acute effects of nitrogen dioxide: they have a higher baseline airway responsiveness. Thus, a nitrogen-dioxide-induced increase in airway responsiveness is expected to have clinical implications

for exaggerated responses to a variety of provocative agents, such as cold air, allergies or exercise. Concern about asthmatics is also enhanced, considering the increase in the number of asthmatics in many countries (many countries have 4–6% asthmatics). A number of epidemiological studies of relatively large populations exposed indoors to peak levels of nitrogen dioxide from gas-combustion appliances have not provided consistent evidence of adverse pulmonary function effects. In one study, elderly women who used gas stoves had a high prevalence of asthma. Nevertheless, the human clinical studies of function and airway reactivity do not show monotonic concentration responses, and the studies are not internally consistent. Animal studies do not provide substantial evidence of biochemical, morphological or physiological effects in the lung following a single acute exposure to concentrations in the range of the lowest-observed-effect level in humans. On the other hand, the mild asthmatics chosen for the controlled exposure studies do not represent all asthmatics, and there are likely to be some individuals with greater sensitivity to nitrogen dioxide. Furthermore, subchronic and chronic animal studies do show significant morphological, biochemical and immunological changes.

The epidemiological studies discussed show increased risk of respiratory illness in children at an increase in nitrogen dioxide level of about 30 $\mu g/m^3$; most studies measured 2-week averages on personal samplers. It is not known, however, whether the effect was related to this 2-week average, the actual pattern (baseline and peaks) over the 2 weeks, the peaks over the 2 weeks, or some other index for a longer time-frame prior to the study measurement. It is also not possible to clearly discern the relative contributions of indoor and outdoor levels of nitrogen dioxide.

Guidelines

Despite the large number of acute controlled exposure studies on humans, several of which used multiple concentrations, there is no evidence for a clearly defined concentration–response relationship for nitrogen dioxide exposure. For acute exposures, only very high concentrations (1990 $\mu g/m^3$; > 1000 ppb) affect healthy people. Asthmatics and patients with chronic obstructive pulmonary disease are clearly more susceptible to acute changes in lung function, airway responsiveness and respiratory symptoms. Given the small changes in lung function (< 5% drop in FEV_1 between air and nitrogen dioxide exposure) and changes in airway responsiveness reported in several studies, 375–565 $\mu g/m^3$ (0.20–0.30 ppm) is a clear lowest-observed-effect level. A 50% margin of safety is proposed because of the reported statistically significant increase in response to a bronchoconstrictor (increased airway responsiveness) with exposure to 190 $\mu g/m^3$ and a

meta-analysis suggesting changes in airway responsiveness below 365 μg/m^3. (The significance of the response at 190 μg/m^3 (100 ppb) has been questioned on the basis of an inappropriate statistical analysis.)

On the basis of these human clinical data, a 1-hour guideline of 200 μg/m^3 is proposed. At double this recommended guideline (400 μg/m^3) there is evidence to suggest possible small effects in the pulmonary function of asthmatics. Should the asthmatic be exposed either simultaneously or sequentially to nitrogen dioxide and an aeroallergen, the risk of an exaggerated response to the allergen is increased. At 50% of the suggested guideline (100 μg/m^3, 50 ppb) there have been no studies of acute response in 1 hour.

Although there is no particular study or set of studies that clearly support selection of a specific numerical value for an annual average guideline, the database nevertheless indicates a need to protect the public from chronic nitrogen dioxide exposure. For example, indoor air studies with a strong nitrogen dioxide source, such as gas stoves, suggest that an increment of about 30 μg/m^3 (2-week average) is associated with a 20% increase in lower respiratory illness in children aged 5–12 years. However, the affected children had a pattern of indoor exposure that included peak exposures higher than those typically encountered outdoors. Thus the results cannot be readily extrapolated quantitatively to the outdoor situation. Outdoor epidemiological studies have found qualitative evidence of ambient exposures being associated with increased respiratory symptoms and lung function decreases in children (most clearly suggestive at annual average concentrations of 50–75 μg/m^3 or higher and consistent with findings from indoor studies), although they do not provide clear exposure–response information for nitrogen dioxide. In these epidemiological studies, nitrogen dioxide has appeared to be a good indicator of the pollutant mixture. Furthermore, animal toxicological studies show that prolonged exposures can cause decreases in lung host defences and changes in lung structure. On these grounds, it is proposed that a long-term guideline for nitrogen dioxide be established. Selecting a well supported value based on the studies reviewed has not been possible, but it has been noted that a prior review conducted for the Environmental Health Criteria document on nitrogen oxides recommended an annual value of 40 μg/m^3 *(5)*. In the absence of support for an alternative value, this figure is recognized as an air quality guideline.

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7.2 Ozone and other photochemical oxidants

Exposure evaluation

Ozone and other photochemical oxidants are formed by the action of short-wavelength radiation from the sun on nitrogen dioxide. In the presence of volatile organic compounds, the equilibrium favours the formation of higher levels of ozone. Background levels of ozone, mainly of anthropogenic origin, are in the range 40–70 μg/m^3 (0.02–0.035 ppm) but can be as high as 120–140 μg/m^3 (0.06–0.07 ppm) for 1 hour. In Europe, maximum hourly ozone concentrations may exceed 300 μg/m^3 (0.15 ppm) in rural areas and 350 μg/m^3 (0.18 ppm) in urbanized regions. Submaximal levels (80–90% of maximum) can occur for 8–12 hours a day for many consecutive days.

Health risk evaluation

Ozone toxicity occurs in a continuum in which higher concentrations, longer exposure duration and greater activity levels during exposure cause greater effects. Short-term acute effects include respiratory symptoms, pulmonary function changes, increased airway responsiveness and airway inflammation. These health effects were statistically significant at a concentration of 160 μg/m^3 (0.08 ppm) for 6.6-hour exposures in a group of healthy exercising adults, with the most sensitive subjects experiencing functional decrements of > 10% within 4–5 hours *(1)*. Controlled exposures of heavily exercising adults or children to an ozone concentration of 240 μg/m^3 (0.l2 ppm) for 2 hours have also been observed to produce decrements in pulmonary function *(2, 3)*. There is no question that substantial acute adverse effects occur with 1 hour of exercising exposure at concentrations of 500 μg/m^3 or higher, particularly in susceptible individuals or subgroups.

Field studies in children, adolescents and young adults have indicated that pulmonary function decrements can occur as a result of short-term exposure to ozone concentrations of 120–240 μg/m^3 and higher. Mobile laboratory studies using ambient air containing ozone have observed associations between changes in pulmonary function in children or asthmatics and ozone concentrations of 280–340 μg/m^3 (0.14–0.17 ppm) with exposures lasting several hours. Respiratory symptoms, especially cough, have been associated with ozone concentrations as low as 300 μg/m^3 (0.15 ppm).

Ozone exposure has also been reported to be associated with increased hospital admissions for respiratory causes and exacerbation of asthma. That these effects are observed both with exposures to ambient ozone (and co-pollutants) and with controlled exposures to ozone alone demonstrates that the functional and symptomatic responses can be attributed primarily to ozone.

A number of studies evaluating rats and monkeys exposed to ozone for a few hours or days have shown alterations in the respiratory tract in which the lowest-observed-effect levels were in the range 160–400 μg/m^3 (0.08–0.2 ppm). These included the potentiation of bacterial lung infections, inflammation, morphological alterations in the lung, increases in the function of certain lung enzymes active in oxidant defences, and increases in collagen content. Long-term exposure to ozone in the range 240–500 μg/m^3 (0.12–0.25 ppm) causes morphological changes in the epithelium and interstitium of the centriacinar region of the lung, including fibrotic changes.

Guidelines

The selection of guidelines for ambient ozone concentrations is complicated by the fact that detectable responses occur at or close to the upper limits of background concentrations. At ozone levels of 200 μg/m^3 and lower (for exposure periods of 1–8 hours) there are statistically significant decrements in lung function, airway inflammatory changes, exacerbations of respiratory symptoms and symptomatic and functional exacerbations of asthma in exercising susceptible people. Functional changes and symptoms as well as increased hospital admissions for respiratory causes are also observed in population studies. Thus it is not possible to base the guidelines on a NOAEL or a LOAEL with an uncertainty factor of more than a small percentage. Thus, selection of a guideline has to be based on the premise that some detectable functional responses are of little or no health concern, and that the number of responders to effects of concern are too few to represent a group warranting protection from exposures to ambient ozone.

In the case of respiratory function responses, a judgement could be made that ozone-related reductions in FEV_1, for example, of < 10% were of no clinical concern. In the case of visits to clinics or emergency departments or hospital admissions for respiratory diseases, it would be necessary to determine how many cases per million population would be needed to constitute a group warranting societal protection. In the case of asthmatic children needing extra medication in response to elevated ozone concentrations, it would be necessary to conclude that medication will be available to sufficiently ameliorate their distress and thereby prevent more serious consequences.

On such a basis, a guideline value for ambient air of 120 μg/m^3 for a maximum period of 8 hours per day is established as a level at which acute effects on public health are likely to be small.

For those public health authorities that cannot accept such levels of health risk, an alternative is to select explicitly some other level of acceptable exposure and associated risk. Tables 22 and 23 summarize the ambient ozone concentrations that are associated with specific levels of response among specified population subgroups. Although chronic exposure to ozone can cause effects, quantitative information from humans is inadequate to estimate the degree of protection from chronic effects offered by this guideline. In any case, the ozone concentration at which any adverse health outcome is expected will vary with the duration of the exposure and the volume of air that is inhaled during the exposure.

Thus, the amount of time spent outdoors and the typical level of activity are factors that should be considered in risk evaluation. Table 22 summarizes the ozone levels at which two representative adverse health outcomes,

Table 22. Health outcomes associated with controlled ozone exposures

Health outcome	Ozone concentration (μg/m^3) at which the health effect is expected	
	Averaging time 1 hour	Averaging time 8 hours
Change in FEV_1 (active, healthy, outdoors, most sensitive 10% of young adults and children):		
5%	250	120
10%	350	160
20%	500	240
Increase in inflammatory changes (neutrophil influx) (healthy young adults at > 40 litres/minute outdoors)		
2-fold	400	180
4-fold	600	250
8-fold	800	320

Table 23. Health outcomes associated with changes in ambient ozone concentration in epidemiological studies

Health outcome	Change in ozone concentration (µg/m³)	
	Averaging time 1 hour	Averaging time 8 hours
Increase in symptom exacerbations among adults or asthmatics (normal activity):		
25%	200	100
50%	400	200
100%	800	300
Increase in hospital admissions for respiratory conditions:[a]		
5%	30	25
10%	60	50
20%	120	100

[a] Given the high degree of correlation between the 1-hour and 8-hour ozone concentration in field studies, the reduction in health risk associated with decreasing 1-hour or 8-hour ozone levels should be almost identical.

based on controlled exposure experiments, may be expected. The concentrations presented in this table have been established by experts on the basis of collective evidence from numerous studies and linear extrapolation in a few cases where data were limited.

Epidemiological data show relationships between changes in various health outcomes and changes in the peak daily ambient ozone concentration. Two examples of such relationships are shown in Table 23. Short-term increases in levels of ambient ozone are associated both with increased hospital admissions with a respiratory diagnosis and respiratory symptom exacerbations, both in healthy people and in asthmatics. These observations may be used to quantify expected improvements in health outcomes that may be associated with lowering the ambient ozone concentration. The values presented in the table assume a linear relationship between ozone concentration and health outcome. Uncertainties exist, however, concerning the forms of these relationships and it is unclear whether similar response slopes can be

expected at widely different ambient ozone levels. In the event that such relationships are curvilinear (concave), the benefits of lowering the ozone concentration are likely to be greater when the average ambient level is higher. Consequently, if the ambient ozone concentration is already low, the benefits of lowering the concentration may be less than would be suggested by Table 23. Another important area of uncertainty is the degree to which other pollutants influence these relationships.

The first edition of *Air quality guidelines for Europe (4)* recommended a 1-hour guideline value of 150–200 μg/m^3. Although recent research does not indicate that this guideline would necessarily be erroneous, the 8-hour guideline would protect against acute 1-hour exposures in this range and thus it is concluded that a 1-hour guideline is not necessary. Furthermore, the health problems of greatest concern (increased hospital admissions, exacerbations of asthma, inflammatory changes in the lung, and structural alterations in the lung) are more appropriately addressed by a guideline value that limits average daily exposure, and consequently inhaled dose and dose rate, rather than one designed to cover the rare short-duration deteriorations in air quality that may be associated with unusual meteorological conditions.

A guideline for peroxyacetyl nitrate is not warranted at present since it does not seem to pose a significant health problem at levels observed in the environment.

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7.3 Particulate matter

Exposure evaluation

Data on exposure levels to airborne inhalable particles are still limited for Europe. Data have mostly been obtained from studies not directly aimed at providing long-term distributions of exposure data for large segments of the population. Nevertheless, it seems that in northern Europe, PM_{10} levels (particulate matter in which 50% of particles have an aerodynamic diameter of less than 10 μm) are low, with winter averages even in urban areas not exceeding 20–30 μg/m^3. In western Europe, levels seem to be higher at 40–50 μg/m^3, with only small differences between urban and non-urban areas. Levels in some central and eastern European locations from which data are available appear nowadays to be only a little higher than those measured in cities such as Amsterdam and Berlin. As a result of the normal day-to-day variation in PM_{10} concentrations, 24-hour averages of 100 μg/m^3 are regularly exceeded in many areas in Europe, especially during winter inversions.

Health risk evaluation

A variety of methods exist to measure particulate matter in air. For the present evaluation, studies have been highlighted in which particulate matter exposure was expressed as the thoracic fraction (~ PM_{10}) or size fractions or constituents thereof. Practically speaking, at least some data are also available on fine particles ($PM_{2.5}$), sulfates and strong aerosol acidity. Health effect studies conducted with (various forms of) total suspended particulates or black smoke as exposure indicators have provided valuable additional information in recent years. They are, however, less suitable for the derivation of exposure–response relationships for particulate matter, because total suspended particulates include particles that are too large to be inhaled or because the health significance of particle opacity as measured by the black smoke method is uncertain.

Recent studies suggest that short-term variations in particulate matter exposure are associated with health effects even at low levels of exposure (below 100 μg/m^3). The current database does not allow the derivation of a threshold below which no effects occur. This does not imply that no threshold exists; epidemiological studies are unable to define such a threshold, if it exists, precisely.

At low levels of (short-term) exposure (defined as 0–100 μg/m^3 for PM_{10}), the exposure–response curve fits a straight line reasonably well. There are

indications from studies conducted in the former German Democratic Republic and in China, however, that at higher levels of exposure (several hundreds of μg/m^3 PM_{10}) the curve is shallower, at least for effects on mortality. In the London mortality studies, there was also evidence of a curvilinear relationship between black smoke and daily mortality, the slope becoming shallower at higher levels of exposure. Estimates of the magnitude of effect occurring at low levels of exposure should therefore not be used to extrapolate to higher levels outside the range of exposures that existed in most of the recent acute health effect studies.

Although there are now many studies showing acute effect estimates of PM_{10} that are quantitatively reasonably consistent, this does not imply that particle composition or size distribution within the PM_{10} fraction is unimportant. Limited evidence from studies on dust storms indicates that such PM_{10} particles are much less toxic than those associated with combustion sources. Recent studies in which PM_{10} size fractions and/or constituents have been measured suggest that the observed effects of PM_{10} are in fact largely associated with fine particles, strong aerosol acidity or sulfates (which may serve as a proxy for the other two) and not with the coarse (PM_{10} minus $PM_{2.5}$) fraction.

Traditionally, particulate matter air pollution has been thought of as a primarily urban phenomenon. It is now clear that in many areas of Europe, urban–rural differences in PM_{10} are small or even absent, indicating that particulate matter exposure is widespread. Indeed, several of the health effect studies reviewed in this chapter were conducted in rural or semirural rather than urban areas. This is not to imply that exposure to primary, combustion-related particulate matter may not be higher in urban areas. At present, however, data are lacking on the specific health risks of such exposures.

Evidence is emerging also that long-term exposure to low concentrations of particulate matter in air is associated with mortality and other chronic effects, such as increased rates of bronchitis and reduced lung function. Two cohort studies conducted in the United States suggest that life expectancy may be shortened by more than a year in communities exposed to high concentrations compared to those exposed to low concentrations. This is consistent with earlier results from cross-sectional studies comparing age-adjusted mortality rates across a range of long-term average concentrations. Again, such effects have been suggested to be associated with long-term average exposures that are low, starting at a concentration of fine particulate matter of about 10 μg/m^3. Whereas such observations require further corroboration, preferably also from other areas in the world, these new studies

suggest that the public health implications of particulate matter exposure may be large.

Evaluation of the effects of short-term exposure on mortality and morbidity

Table 24 shows the summary estimates of relative increase in daily mortality, respiratory hospital admissions, reporting of bronchodilator use, cough and lower respiratory symptoms, and changes in peak expiratory flow associated with a 10 μg/m^3 increase in PM_{10} or $PM_{2.5}$, as reported in studies in which PM_{10} and/or $PM_{2.5}$ concentrations were actually measured (as opposed to being inferred from other measures such as coefficient of haze, black smoke or total suspended particulates). The database for parameters other than PM_{10} is still limited, but for the reasons noted above, it is very important to state that even though the evaluation of (especially the short-term) health effects is largely expressed in terms of PM_{10}, future regulations and monitoring activities should place emphasis on (appropriate representations of) the respiratory fraction in addition to, or even preferred to, PM_{10} *(1)*.

It is important to realize that at present it is not known what reduction in life expectancy is associated with daily mortality increases related to particulate matter exposure. If effects are restricted to people in poor health, effects on age at death may be small.

Table 24. Summary of relative risk estimates for various endpoints associated with a 10 μg/m^3 increase in the concentration of PM_{10} or $PM_{2.5}$

Endpoint	Relative risk for $PM_{2.5}$ (95% confidence interval)	Relative risk for PM_{10} (95% confidence interval)
Bronchodilator use		1.0305 (1.0201–1.0410)
Cough		1.0356 (1.0197–1.0518)
Lower respiratory symptoms		1.0324 (1.0185–1.0464)
Change in peak expiratory flow (relative to mean)		–0.13% (–0.17% to –0.09%)
Respiratory hospital admissions		1.0080 (1.0048–1.0112)
Mortality	1.015 (1.011–1.019)	1.0074 (1.0062–1.0086)

The effect estimates in Table 24 can be used with considerable reservation to estimate, for a population of a given size and mortality and morbidity experience, how many people would be affected over a short period of time with increased particulate matter levels. The reservation stems from the finding that for some of the estimated effects, there was no evidence of heterogeneity between studies in the magnitude of the effect estimate. An investigation of the reasons for heterogeneity is beyond the scope of this chapter. As a consequence, the pooled effect estimates may not be applicable in all possible circumstances.

For illustrative purposes, Table 25 contains an estimate of the effect of a 3-day episode with daily PM_{10} concentrations averaging 50 µg/m^3 and 100 µg/m^3 on a population of 1 million people. Table 25 makes it clear that, in a population of that size, the number of people dying or having to be admitted to hospital as a result of particulate matter exposure is small relative to the additional number of "person-days" of increased medication use and/or increased respiratory symptoms due to exposure to particulate matter.

Whereas these calculations should be modified according to the size, mortality and morbidity experience of populations of interest and, where possible, for factors contributing to the heterogeneity in the effect estimates, they do provide some insight into the public health consequences of certain exposures to particulate matter.

Table 25. Estimated number of people (in a population of 1 million) experiencing health effects over a period of 3 days characterized by a mean PM_{10} concentration of 50 or 100 µg/m^3

Health effect indicator	No. of people affected by a three-day episode of PM_{10} at:	
	50 µg/m^3	100 µg/m^3
No. of deaths	4	8
No. of hospital admissions due to respiratory problems	3	6
Person-days of bronchodilator use	4 863	10 514
Person-days of symptom exacerbation	5 185	11 267

Evaluation of the effects of long-term exposure on mortality and morbidity

The most convincing information on long-term effects of particulate matter exposure on mortality is provided by two recent cohort studies. Relative risk estimates for total mortality from the first study *(2)*, expressed per 10 μg/m^3, were 1.10 for inhalable particles (measured as either PM_{15} or PM_{10}), 1.14 for fine particles ($PM_{2.5}$) and 1.33 for sulfates. Relative risk estimates for total mortality from the second study *(3)*, expressed per 10 μg/m^3, were 1.07 for fine particles ($PM_{2.5}$) and 1.08 for sulfates. Sulfate levels used in the second study (range 3.6–23.6 μg/m^3) may have been inflated owing to sulfate formation on filter material used in earlier studies. The first study included one of the high-sulfate communities (Steubenville), yet the range of sulfate levels in this study was much lower (4.8–12.8 μg/m^3), possibly owing to the more adequate measurement methods employed in this study.

Long-term effects of particulate matter exposure on morbidity have been demonstrated in the Harvard 24 cities study among children *(4, 5)*. Expressed per 10 μg/m^3, the relative risks for bronchitis were 1.34 for $PM_{2.1}$, 1.29 for PM_{10}, and 1.96 for sulfate particles. The corresponding changes in FEV_1 were –1.9% ($PM_{2.1}$), –1.2% (PM_{10}) and –3.1% (sulfate particles). Whereas such mean changes are clinically unimportant, the proportion of children having a clinically relevant reduced lung function (forced vital capacity (FVC) or FEV_1 < 85% of predicted) was increased by a factor of 2–3 across the range of exposures *(5)*. A recent study from Switzerland *(6)* has shown significant reductions in FEV_1 of –1.0% per 10 μg/m^3 PM_{10}.

Table 26 provides a summary of the current knowledge of effects of long-term exposure to particulate matter on morbidity and mortality endpoints.

Using the risk estimates presented in Table 26, Table 27 provides estimates of the number of people experiencing health effects associated with long-term exposure to particulate matter, using similar assumptions about population size and morbidity as in Table 25. Specifically, a population size of one million has been assumed, 20% of whom are children, with a baseline prevalence of 5% for bronchitis symptoms among children (that is, 10 000 children are assumed to have bronchitis symptoms) and with a baseline prevalence of 3% of children (6000 children) having a lung function (FVC or FEV_1) lower than 85% of predicted.

In addition, the impact of long-term exposures to particulate matter on total mortality can be estimated. The number of persons surviving to a

Table 26. Summary of relative risk estimates for effects of long-term exposure to particulate matter on the morbidity and mortality associated with a 10 μg/m³ increase in the concentration of $PM_{2.5}$ or PM_{10}

Endpoint	Relative risk for $PM_{2.5}$ (95% confidence interval)	Relative risk for PM_{10} (95% confidence interval)
Death *(2)*	1.14 (1.04–1.24)	1.10 (1.03–1.18)
Death *(3)*	1.07 (1.04–1.11)	
Bronchitis *(4)*	1.34 (0.94–1.99)	1.29 (0.96–1.83)
Percentage change in FEV_1, children *(5)* [a]	–1.9% (–3.1% to –0.6%)	–1.2% (–2.3% to –0.1%)
Percentage change in FEV_1, adults *(6)*		–1.0% (not available)

[a] For $PM_{2.1}$ rather than $PM_{2.5}$.

Table 27. Estimated number of children (out of 200 000 in a population of 1 million) experiencing health effects per year due to long-term exposure to a $PM_{2.5}$ concentration of 10 or 20 μg/m³ above a background level of 10 μg/m³

Health effect indicator	No. of children affected per year at $PM_{2.5}$ concentrations above background of:	
	10 μg/m³	20 μg/m³
No. of additional children with bronchitis symptoms	3350	6700
No. of additional children with lung function (FVC or FEV_1) below 85% of predicted	4000	8000

certain age will be smaller in a population exposed to higher concentrations, and the difference will depend on the age group. If the mortality structure of Dutch males is taken as a basis for calculation, and if the assumptions used in the construction of Table 25 are applied, in each birth cohort of 100 000 men the number of survivors exposed to pollution increased by 10 μg/m³ (PM_{10}) will be reduced by 383 men before the age of 50, by 1250 men before the age of 60 and by 3148 men before the age of 70. An

increase in the long-term exposure of 20 μg/m^3 (PM_{10}) corresponds to an estimated reduction of the number of men surviving to a certain age in the cohorts by, respectively, 764, 2494 or 6250 men.

Guidelines

The weight of evidence from numerous epidemiological studies on short-term responses points clearly and consistently to associations between concentrations of particulate matter and adverse effects on human health at low levels of exposure commonly encountered in developed countries. The database does not, however, enable the derivation of specific guideline values at present. Most of the information that is currently available comes from studies in which particles in air have been measured as PM_{10}. There is now also a sizeable body of information on fine particulate matter ($PM_{2.5}$) and the latest studies are showing that this is generally a better predictor of health effects than PM_{10}. Evidence is also emerging that constituents of $PM_{2.5}$ such as sulfates are sometimes even better predictors of health effects than $PM_{2.5}$ *per se*.

The large body of information on studies relating day-to-day variations in particulate matter to day-to-day variations in health provides quantitative estimates of the effects of particulate matter that are generally consistent. The available information does not allow a judgement to be made of concentrations below which no effects would be expected. Effects on mortality, respiratory and cardiovascular hospital admissions and other health variables have been observed at levels well below 100 μg/m^3, expressed as a daily average PM_{10} concentration. For this reason, no guideline value for short-term average concentrations is recommended either. Risk managers are referred to the risk estimates provided in the tables for guidance in decision-making regarding standards to be set for particulate matter.

The body of information on long-term effects is still smaller. Some studies have suggested that long-term exposure to particulate matter is associated with reduced survival, and a reduction of life expectancy in the order of 1–2 years. Other recent studies have shown that the prevalence of bronchitis symptoms in children, and of reduced lung function in children and adults, are associated with particulate matter exposure. These effects have been observed at annual average concentration levels below 20 μg/m^3 (as $PM_{2.5}$) or 30 μg/m^3 (as PM_{10}). For this reason, no guideline value for long-term average concentrations is recommended. Risk managers are referred to the risk estimates provided in the tables for guidance in decision-making regarding standards to be set for particulate matter.

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7.4 Sulfur dioxide

Exposure evaluation

In much of western Europe and North America, concentrations of sulfur dioxide in urban areas have continued to decline in recent years as a result of controls on emissions and changes in fuel use. Annual mean concentrations in such areas are now mainly in the range 20–60 μg/m^3 (0.007–0.021 ppm), with daily means seldom more than 125 μg/m^3 (0.044 ppm). In large cities where coal is still widely used for domestic heating or cooking, however, or where there are poorly controlled industrial sources, concentrations may be 5–10 times these values. Peak concentrations over shorter averaging periods, of the order of 10 minutes, can reach 1000–2000 μg/m^3 (0.35–0.70 ppm) in some circumstances, such as the grounding of plumes from major point sources or during peak dispersion conditions in urban areas with multiple sources.

Health risk evaluation

Short-term exposures (less than 24 hours)

The most direct information on the acute effects of sulfur dioxide comes from controlled chamber experiments on volunteers. Most of these studies have been for exposure periods ranging from a few minutes up to 1 hour, but the exact duration is not critical because responses occur very rapidly, within the first few minutes after commencement of inhalation; continuing the exposure further does not increase effects *(1–3)*. The effects observed include reductions in FEV_1 or other indices of ventilatory capacity, increases in specific airway resistance, and symptoms such as wheezing or shortness of breath. Such effects are enhanced by exercise, which increases the volume of air inspired thereby allowing sulfur dioxide to penetrate further into the respiratory tract *(4, 5)*.

A wide range of sensitivity has been demonstrated, both among normal individuals and among those with asthma, who form the most sensitive group *(1, 4, 6, 7)*. Continuous exposure–response relationships, without any clearly defined threshold, are evident. To develop a guideline value, the minimum concentrations associated with adverse effects in the most extreme circumstances, that is with asthmatic patients exercising in chambers, have been considered. An example of an exposure–response relationship for such subjects, expressed in terms of reductions in FEV_1 after a 15-minute exposure, comes from a study by Linn et al. (*8*). Only small changes, not

regarded as of clinical significance, were seen at 572 μg/m^3 (0.2 ppm); reductions representing about 10% of baseline FEV_1 occurred at about 1144 μg/m^3 (0.4 ppm); and reductions of about 15% occurred at about 1716 μg/m^3 (0.6 ppm). The response was not greatly influenced by the severity of asthma. These findings are consistent with those reported from other exposure studies. In one early series, however, a small change in airway resistance was reported in two of the asthmatic patients at 286 μg/m^3 (0.1 ppm).

Exposure over a 24-hour period

Information on effects of exposure averaged over a 24-hour period is derived mainly from epidemiological studies in which the effects of sulfur dioxide, particulate matter and other associated pollutants are considered *(9)*. Exacerbation of symptoms among panels of selected sensitive patients occurred consistently when the sulfur dioxide concentration exceeded 250 μg/m^3 (0.087ppm) in the presence of particulate matter. Such findings have related mainly to situations in which emissions from the inefficient burning of coal in domestic appliances have been the main contributor to the pollution complex. Several more recent studies, involving the mixed industrial and vehicular sources that now dominate, have consistently demonstrated effects on mortality (total, cardiovascular and respiratory) *(10–18)* and hospital emergency admissions *(14, 19–22)* for total respiratory causes and chronic obstructive pulmonary disease at lower levels of exposure (mean annual levels below 50 μg/m^3; daily levels usually not exceeding 125 μg/m^3). These results have been shown, in some instances, to persist when levels of black smoke and total suspended particulate matter were controlled for, while in other studies no attempts were made to separate the effects of the pollutants. No obvious threshold levels could so far be identified in those studies.

Long-term exposure

A similar situation arises in respect of effects of long-term exposures, expressed as annual averages. Earlier assessments examined findings on the prevalence of respiratory symptoms, respiratory illness frequencies, or differences in lung function values in localities with contrasting concentrations of sulfur dioxide and particulate matter, largely in the coal-burning era. The LOAEL of sulfur dioxide was judged to be 100 μg/m^3 (0.035 ppm) annual average, together with particulate matter. More recent studies related to industrial sources, or to the changed urban mixture, have shown adverse effects below this level, but a major difficulty in interpretation is that long-term effects are liable to be affected not only by current conditions but also by the qualitatively and quantitatively different pollution of

earlier years. Cohort studies of differences in mortality between areas with contrasting pollution levels indicate that there is a closer association with particulate matter than with sulfur dioxide *(23, 24)*.

Guidelines

Short-term exposures

Controlled studies with exercising asthmatics indicate that some asthmatics experience changes in pulmonary function and respiratory symptoms after periods of exposure as short as 10 minutes. Based on this evidence, it is recommended that a value of 500 μg/m^3 (0.175 ppm) should not be exceeded over averaging periods of 10 minutes. Because exposure to sharp peaks depends on the nature of local sources, no single factor can be applied to this value in order to estimate corresponding guideline values over somewhat longer periods, such as an hour.

Exposure over a 24-hour period and long-term exposure

Day-to-day changes in mortality, morbidity or lung function related to 24-hour average concentrations of sulfur dioxide are necessarily based on epidemiological studies in which people are in general exposed to a mixture of pollutants, which is why guideline values for sulfur dioxide have previously been linked with corresponding values for particulate matter. This approach led to a previous guideline value of 125 μg/m^3 (0.04 ppm) as a 24-hour average, after applying an uncertainty factor of 2 to the LOAEL. In more recent studies, adverse effects with significant public health importance have been observed at much lower levels of exposure. Nevertheless, there is still uncertainty as to whether sulfur dioxide is the pollutant responsible for the observed adverse effects or, rather, a surrogate for ultrafine particles or some other correlated substance. There is no basis for revising the 1987 guidelines for sulfur dioxide *(9)* and thus the following guidelines are recommended:

24 hours:	125 μg/m^3
annual:	50 μg/m^3

It should be noted that, unlike in the 1987 guidelines, these values for sulfur dioxide are no longer linked with particles.

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CHAPTER 8

Indoor air pollutants

8.1 Environmental tobacco smoke

Exposure evaluation

Environmental tobacco smoke (ETS) is a dynamic complex mixture of thousands of compounds in particulate and vapour phases, and cannot be measured directly as a whole. Instead, various marker compounds, such as nicotine and respirable suspended particulates (RSPs), are used to quantify environmental exposure. In the United States, nicotine concentrations in homes where smoking occurs typically range from less than 1 μg/m^3 to over 10 μg/m^3 (*1*). Concentrations in offices where people smoke typically range from near zero to over 30 μg/m^3. Levels in restaurants, and especially bars, tend to be even higher, and concentrations in confined spaces such as cars can be higher still. Measurements of ETS-associated RSPs in homes where people smoke range from a few μg/m^3 to over 500 μg/m^3, while levels in offices are generally less than 100 μg/m^3 and those in restaurants can exceed 1 mg/m^3. ETS levels are directly related to smoker density; in countries with a higher smoking prevalence, average ETS levels could be higher.

In Western societies, with adult smoking prevalences of 30–50%, it is estimated that over 50% of homes are occupied by at least one smoker, resulting in a high prevalence of ETS exposure in children and other nonsmokers. A large percentage of nonsmokers are similarly exposed at work.

Health risk evaluation

ETS has been shown to increase the risks for a variety of health effects in nonsmokers exposed at typical environmental levels. The pattern of health effects from ETS exposure produced in adult nonsmokers is consistent with the effects known to be associated with active cigarette smoking. Chronic exposures to ETS increase lung cancer mortality *(1–5)*. In addition, the combined evidence from epidemiology and studies of mechanisms leads to the conclusion that ETS increases the risk of morbidity and mortality from cardiovascular disease in nonsmokers, especially those with chronic exposure *(4, 6–11)*. ETS also irritates the eyes and respiratory tract. In infants and young children, ETS increases the risk of pneumonia, bronchitis, bronchiolitis and fluid in the middle ear *(1, 2, 13, 14)*. In asthmatic children, ETS increases the severity and frequency of asthma attacks *(12)*. Furthermore, as with active smoking, ETS reduces birth weight in the offspring of nonsmoking mothers *(15)*.

Other health effects have also been associated with ETS exposure, but the evidence is not as conclusive. In adults, there is strong suggestive evidence that ETS increases mortality from sinonasal cancer *(16, 17)*. In infants, recent evidence suggests that ETS is a risk factor for sudden infant death syndrome *(18–22)*.

Populations at special risk for the adverse health effects of ETS are young children and infants, asthmatics, and adults with other risk factors for cardiovascular disease. Levels of exposure where these effects have been observed are indicated by nicotine levels of 1–10 $\mu g/m^3$ (nicotine has been demonstrated to be a reliable marker of ETS levels).

Because of the extensive prevalence of ETS exposure and the high incidence of some of the health effects associated with ETS exposure, such as cardiovascular disease in adults and lower respiratory tract infections in children, even small increases in relative risks can translate into substantial levels of mortality and morbidity on a population basis.

Based on the combined evidence from several studies, WHO has estimated that some 9–13% of all cancer cases can be attributed to ETS in a nonsmoking population of which 50% are exposed to ETS. The proportion of lower respiratory illness in infants attributed to ETS exposure can be estimated at 15–26%, assuming that 35% of the mothers smoke at home. Those estimates, when applied to the European population, will result in approximately 3000–4500 cases of cancer in adults per year, and between 300 000 and 550 000 episodes of lower respiratory illness in infants per year, which are expected to be related to ETS exposure *(23)*.

Comparable results were calculated for nonsmokers in the United States *(1)*. The US Environmental Protection Agency (EPA) recently estimated that ETS causes 3000 lung cancer deaths in adult nonsmokers (roughly 100 million people who have never smoked and long-term former smokers) in the United States each year. The EPA also estimated that ETS is responsible for between 150 000 and 300 000 lower respiratory tract infections annually in the roughly 5.5 million children under 18 months of age, and that it exacerbates asthma in about 20% of asthmatic children. These estimates are based on a large quantity of human data from actual exposure levels, and involve no high-to-low-dose or animal-to-human extrapolations; thus confidence in these estimates is considered high.

Quantitative population estimates for cardiovascular disease mortality are less certain than those for lung cancer. The main reasons for greater quantitative

uncertainty in estimates for cardiovascular disease are that (*a*) there are fewer epidemiological data available (in particular, there are few data for males, which is especially critical because males have a very different baseline risk of cardiovascular disease than females), and (*b*) there are more risk factors for cardiovascular disease that need to be adjusted for to obtain a reliable risk estimate. In general, the relative risk estimates for cardiovascular disease from ETS exposure are similar to those for lung cancer; however, the baseline risk of death from cardiovascular disease in nonsmokers is at least 10 times higher than the risk of lung cancer. Therefore, the population risks could be roughly 10 times higher as well. Thus, while there is more confidence in the presented estimates for lung cancer, the public health impact of ETS is expected to be substantially greater for cardiovascular disease.

Guidelines

ETS has been found to be carcinogenic in humans and to produce a substantial amount of morbidity and mortality from other serious health effects at levels of 1–10 $\mu g/m^3$ nicotine (taken as an indicator of ETS). Acute and chronic respiratory health effects on children have been demonstrated in homes with smokers (nicotine 1–10 $\mu g/m^3$) and even in homes with occasional smoking (0.1–1 $\mu g/m^3$). There is no evidence for a safe exposure level. The unit risk of cancer associated with lifetime ETS exposure in a home where one person smokes is approximately 1×10^{-3}.

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8.2 Man-made vitreous fibres

Exposure evaluation

Airborne concentrations during the installation of insulation comprising man-made vitreous fibres (MMVF) are in the range 10^5–2×10^6 fibres/m^3 *(1)*, which is generally higher than the concentrations of about 10^5 fibres/m^3 reported for production plants *(2)*. Little information is available on ambient concentrations of MMVF. A few limited studies of MMVF in outdoor air have reported concentrations ranging from 2 fibres/m^3 in a rural area to 1.7×10^3 fibres/m^3 near a city *(3–5)*. These levels are estimated to represent a very small percentage of the total fibre and total suspended particulate concentrations in the ambient air.

Health risk evaluation

MMVF of diameters greater than 3 μm can cause transient irritation and inflammation of the skin, eyes and upper airways *(6)*.

The deep lung penetration of various MMVF varies considerably, as a function of the nominal diameter of the material. For the six categories of MMVF considered here (continuous filament fibre glass, glass wool fibres, rock wool fibres, slag wool fibres, refractory ceramic fibres and special purpose fibres (glass microfibres)), the potential for deep lung penetration is greatest for refractory ceramic fibres and glass microfibres; both of these materials are primarily used in industrial applications.

In two large epidemiological studies, there have been excesses of lung cancer in rock/slag wool production workers, but not in glass wool, glass microfibre or continuous filament production workers. There have been no increases in the incidence of mesotheliomas in epidemiological studies of MMVF production workers *(7, 8)*. Although concomitant exposure to other substances may have contributed to the observed increase in lung cancer in the rock/slag wool production sector, available data are consistent with the hypothesis that the fibres themselves are the principal determinants of risk. Increases in tumour incidence have not been observed in inhalation studies in animals exposed to rock/slag wool, glass wool or glass microfibre, though they have occurred following intracavitary administration. Available data concerning the effects of continuous filament in animals are limited.

Several types of refractory ceramic fibre have been clearly demonstrated to be carcinogenic in inhalation studies in animal species, inducing

dose-related increased incidence of pulmonary tumours and mesotheliomas in rats and hamsters *(9–11)*. Increased tumour incidence has also been observed following intratracheal *(12)* and intrapleural and intraperitoneal *(13)* administration in animals.

Though uses of refractory ceramic fibres are restricted primarily to the industrial environment, a unit cancer risk for lung tumours for refractory ceramic fibres has been calculated as 1×10^{-6} per fibre/l (for fibre length > 5 μm, and aspect ratio (ratio of fibre length to fibre diameter) of 3:1 as determined by optical microscopy) based on inhalation studies in animals *(14)*.

Guidelines

IARC classified rock wool, slag wool, glass wool and ceramic fibres in Group 2B (possibly carcinogenic to humans) while glass filaments were not considered classifiable as to their carcinogenicity to humans (Group 3) *(15)*. Recent data from inhalation studies in animals strengthen the evidence for the possible carcinogenicity of refractory ceramic fibres in humans.

Though uses of refractory ceramic fibres are restricted primarily to the industrial environment, the unit risk for lung tumours is 1×10^{-6} per fibre/l. The corresponding concentrations of refractory ceramic fibres producing excess lifetime risks of 1/10 000, 1/100 000 and 1/1 000 000 are 100, 10 and 1 fibre/l, respectively.

For most other MMVF, available data are considered inadequate to establish air quality guidelines.

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8.3 Radon

Exposure evaluation

Exposure to radon and radon progeny is the dominant source of exposure to ionizing radiation in most countries. The radon levels vary considerably between dwellings, and depend primarily on the inflow of soil gas and the type of building material. As shown in Table 28, arithmetic mean concentrations in European countries range from about 20 Bq/m^3 to 100 Bq/m^3, with even higher levels in some regions. The geometric mean concentrations are generally about 20–50% lower because of the skewed distribution of radon levels.

Health risk evaluation

A few recent case-control studies provide evidence on lung cancer risks related to residential radon exposure. In general, the exposure assessment was based on radon measurements in the homes of the people being studied, covering residential periods of about 10–30 years *(1)*. Some of the studies indicate increased relative risks for lung cancer by estimated time-weighted residential radon level or cumulative exposure, but the picture is not fully coherent. It should be realized, however, that most studies lacked an adequate statistical power. The largest of the studies, with analyses over the widest range of exposure, showed a clear increase in risk with estimated exposure to radon, which appeared consistent with a linear relative risk model *(2)*. The interaction between radon exposure and smoking with regard to lung cancer exceeded additivity and was close to a multiplicative effect.

To date, risk estimation for residential radon exposure has often been based on extrapolation of findings in underground miners. Several circumstances make such estimates uncertain for the general population, however, including the possible influence of other exposure factors in the mines and differences in age, sex, size distribution of aerosols, the attached fraction of radon progeny, breathing rate and route *(3, 4)*. Furthermore, the relevance is not fully understood of the apparent inverse effect of exposure rate observed in miners and the possible difference in relative risk estimates for nonsmokers and smokers *(5)*.

It is of interest to compare risk estimates based on the nationwide Swedish study on residential radon exposure and lung cancer *(2)* with those obtained from miners. Fig. 1 shows the estimated attributable proportion of lung

Table 28. Radon levels in dwellings of some European countries

				Radon concentration (Bq/m^3)					
Country	**Number of Houses sampled**	**Period and duration of exposure**	**Sample characteristics**	**Average**	**Geometric mean**	**Geometric mean SD[a]**	**Percentage over 200 Bq/m^3**	**Percentage over 400 Bq/m^3**	**Reference**
Belgium	300	1984–1990 3 months to 1 year	Population -based (selected acquaintances)	48	37	1.9	1.7	0.3	[b]
Czecho slovakia	1200	1982 random grab sampling	–	140	–	–	–	–	*(7)*
Denmark	496	1985–1986 6 months	random	47	29	2.2	2.2	< 0.4	*(8)*
Finland	3074	1990–1991 1 year	random	123	84	2.1	12.3	3.6	*(9)*
France	1548	1982–1991 3 months (using open alpha track detectors)	biased (not stratified)	85	52	2.3	7.1	2.3	*(10)*
Germany	7500	1978–1984 3 months 1991–1993 1 year	random	50	40	–	1.5–2.5	0.5–1	*(11,12)*

Greece	73	1988 6 months	–	52	–	–	–	–	*(7)*
Hungary	122	1985–1987 2.5 years	preliminary survey	55	42 (median)	–	–	–	[c]
Ireland	1259	1985–1989 6 months	random	60	34	2.5	3.8	1.6	*(13)*
Italy	4866	1989–1994 1 year	stratified random	75	62	2.0	4.8	1.0	*(14)*
Luxembourg	2500	1991	–	–	65	–	–	–	*(7)*
Netherlands	1000	1982–1984 1 year	random	29	24 (median)	1.6	–	–	*(7,15)*
Norway	7525	1987–1989 6 months	random	60	32	–	5.0	1.6	*(16)*
Portugal	4200	1989–1990 1–3 months	volunteers in a selected group (high school students)	81	37	–	8.6	2.6	*(17)*
Spain	1555–2000	winter of 1988– 1989 grab sampling	random	86	41–43	2.6–3.7	–	4	*(7,18)*
Sweden	1360	1982–1992 3 months in heating season	random	108	56	–	14	4.8	*(19)*

Table 28. (contd)

Switzerland	1540	1982–1990 3 months (mainly in winter)	biased (not stratified)	70	–	–	5.0	–	*(20)*
United Kingdom	2093	1986–1987 1 year	random	20.5	15	2.2	0.5	0.2	*(21)*

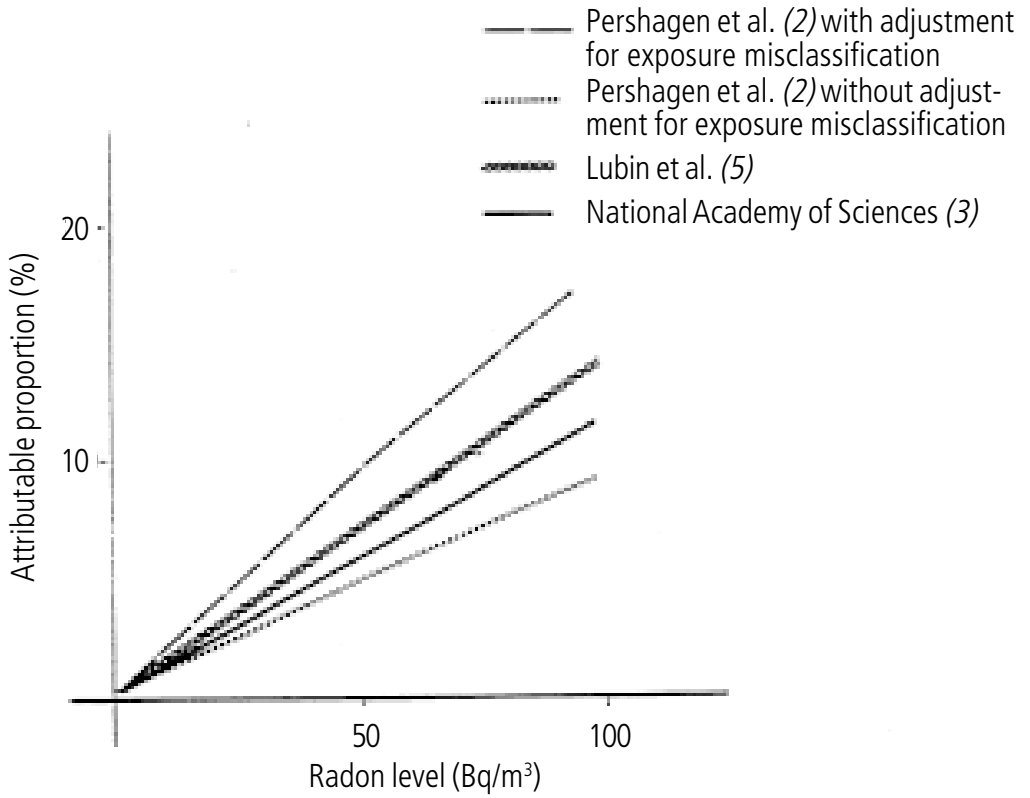
[a] SD = Standard deviation.

[b] A. Poffjin, personal communication.

[c] L. Sztanyik & I. Nikl, personal communication.

Source: Bochicchio et al. *(22)*.

Fig. 1. Estimated attributable proportion of lung cancer related to residential radon exposure based on the national Swedish study and extrapolations from miners



cancer related to residential radon, using risk estimates from the Swedish study and assuming a linear relative risk model. Imprecision in the exposure estimation leads to attenuation of the exposure–response relationship, and it has been indicated that this may have led to an underestimation of the risk by a factor of up to about 2 *(6)*. It is suggested that the true values lie between the unadjusted and adjusted estimates.

Fig. 1 also gives estimates of attributable proportion based on extrapolations from underground miners, after adjusting for dosimetric differences between mines and homes. As an example, the radon concentration distribution in western Germany, with an arithmetic mean of 50 Bq/m^3, leads to an attributable proportion of 7% (95% confidence interval: 1–29%) using the model in Lubin et al. *(5)*, and 6% (95% confidence interval: 2–17%) using that of the National Academy of Sciences *(3)*. Corresponding values based on the Swedish residential study are 5% and 9%, respectively, without and with adjustment for exposure misclassification.

Table 29 shows population risk estimates under three different assumptions with regard to population exposure, taken to represent long-term residential exposure in European countries with relatively high, medium and low residential radon concentrations. The estimated attributable proportion of lung cancer related to residential radon exposure ranges from 2–5% in low-exposure areas to 9–17% in high-exposure areas.

Table 29 also shows estimated excess lifetime deaths from lung cancer related to residential radon. Assuming that lung cancer deaths constitute 3% of total deaths, it is estimated that around 600–1500 excess lung cancer deaths occur per million people exposed on average to

Table 29. Attributable proportion of lung cancer related to long-term residential radon exposure in regions with high, medium and low indoor concentrations [a]

	Concentration		
	High	**Medium**	**Low**
Radon concentration			
Arithmetic mean (Bq/m^3)	100	50	25
> 200 Bq/m^3	15%	1.5%	0.75%
> 400 Bq/m^3	5%	0.5%	0.25%
Proportion of all lung cancers attributable to the exposure			
Total	9–17% [b]	5–9%	2–5%
> 200 Bq/m^3	4–6%	0.4–0.6%	0.2–0.3%
> 400 Bq/m^3	2–3%	0.2–0.3%	0.1–0.15%
Excess lifetime lung cancer deaths (per million) [c]			
Total	2700–5100	1500–2700	600–1500
> 200 Bq/m^3	1200–1800	120–180	60–90
> 400 Bq/m^3	600–900	60–90	30–45

[a] A linear relative risk model is assumed and a multiplicative interaction between radon and other risk factors for lung cancer, including smoking.

[b] The range in estimated attributable proportion is based on assessment of the uncertainty due to imprecision in exposure estimates of the observed exposure–response relationship *(6)*.

[c] It is assumed that lung cancer deaths constitute 3% of total deaths.

Source: Pershagen et al. *(2)*.

25 Bq/m^3 over their lifetime. For an average exposure of 100 Bq/m^3, the corresponding estimate ranges from 2700 to 5100 excess lung cancer deaths per million people exposed.

Guidelines

Radon is a known human carcinogen (classified by IARC as Group 1 *(23)*) with genotoxic action. No safe level of exposure can be determined. Quantitative risk estimates may be obtained from a recent large residential study, which are in general agreement with a linear extrapolation of risks observed in miners. The risk estimates obtained in the studies conducted among miners and the recent study from Sweden *(2)* would correspond to a unit risk of approximately 3–6 × 10^{-5} per Bq/m^3, assuming a lifetime risk of lung cancer of 3%. This means that a person living in an average European house with 50 Bq/m^3 has a lifetime excess lung cancer risk of 1.5–3 × 10^{-3}. Similarly, a person living in a house with a high radon concentration of 1000 Bq/m^3 has a lifetime excess lung cancer risk of 30–60 × 10^{-3} (3–6%), implying a doubling of background lung cancer risk.

Current levels of radon in dwellings and other buildings are of public health concern. A lifetime lung cancer risk below about 1 × 10^{-4} cannot be expected to be achievable because natural concentration of radon in ambient outdoor air is about 10 Bq/m^3. No guideline value for radon concentration is recommended. Nevertheless, the risk can be reduced effectively based on procedures that include optimization and evaluation of available control techniques. In general, simple remedial measures should be considered for buildings with radon progeny concentrations of more than 100 Bq/m^3 equilibrium equivalent radon as an annual average, with a view to reducing such concentrations wherever possible.

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PART III

EVALUATION OF ECOTOXIC EFFECTS

CHAPTER 9

General approach

In the context of the updating and revision of these guidelines, the ecological effects of major air pollutants were considered in more detail. This was undertaken in cooperation with the Working Group on Effects under the United Nations Economic Commission for Europe (ECE) Convention on Long-range Transboundary Air Pollution, capitalizing on the scientific work undertaken since 1988 to formulate criteria for the assessment of the effects of air pollutants on the natural environment.

The evaluation for the guidelines focused on the ecological effects of sulfur dioxide (including sulfur and total acid deposition), nitrogen dioxide (and other nitrogen compounds including ammonia) and ozone, which were thought to be currently of greatest concern across Europe. A number of other atmospheric contaminants are known to have ecological effects, but were not considered by the working groups. In the case of metals and persistent organic pollutants, levels of soil contamination or bioaccumulation leading to adverse effects have been proposed, but methods of linking these to atmospheric concentrations or depositions have not yet been developed. In the case of fluorides and particles, ecological effects are no longer of widespread concern in Europe, although air quality criteria have been proposed in the past by other bodies, and new criteria for fluorides are currently under consideration by certain national governments.

USE OF THE GUIDELINES IN PROTECTING THE ENVIRONMENT

Although the main objective of the guidelines is the direct protection of human health, the WHO strategy for health for all recognizes the importance of protecting the environment in terms of benefits to human health and wellbeing. Resolution WHA42.26 of the World Health Assembly and resolutions 42/187 and 42/186 of the United Nations General Assembly recognize the interdependence of health and the environment.

Ecologically based guidelines for preventing adverse effects on terrestrial vegetation were included for the first time in the first edition of *Air quality guidelines for Europe* in 1987, and guidelines were recommended for some

gaseous air pollutants. Since that time, however, significant advances have been made in the scientific understanding of the impacts of air pollutants on the environment. The realization that soils play an important role in mediating both the direct and indirect effects of air pollutants on terrestrial and freshwater ecosystems has led to the development and acceptance of the joint concepts of critical levels and critical loads within the framework of the ECE Convention on Long-range Transboundary Air Pollution.

At the ECE Workshop on Critical Loads for Sulphur and Nitrogen, held at Skokloster, Sweden *(1)* and at a workshop on critical levels held at Bad Harzburg, Germany *(2)*, the following definitions were agreed on.

Critical level is the concentration of pollutants in the atmosphere above which direct adverse effects on receptors such as plants, ecosystems or materials may occur according to present knowledge.

Critical load is a quantitative estimate of an exposure, in the form of deposition, to one or more pollutants below which significant harmful effects on specified sensitive elements of the environment do not occur according to present knowledge.

The critical levels and loads approach is essentially a further development of the first edition of these guidelines published in 1987. There are several fundamental differences between conventional environmental objectives, critical levels and critical loads (Table 30).

Critical levels relate to direct effects on plant physiology, growth and vitality, and are expressed as atmospheric concentrations or cumulative exposures over a given averaging time. Typically, critical levels are based on effects observed over periods of from one day to several years. Critical loads relate to effects on ecosystem structure and functioning, and are expressed as annual depositions of mass or acidity. Typically, critical loads relate to the potential effects over periods of decades. In the case of sulfur and nitrogen compounds, critical levels can be directly related to critical loads when the deposition velocity for a given vegetation type is known. Nevertheless, while critical levels provide effects thresholds for relatively short-term exposures, and are not aimed at providing complete protection of all plants in all situations from adverse effects, critical loads provide the long-term deposition below which we are sure that adverse ecosystem effects will not occur.

Both critical levels and critical loads may be used to indicate the state of existing or required environmental protection, and they have been used by

Table 30. Differences between conventional environmental objectives, critical levels and critical loads

Conventional objectives	Critical levels	Critical loads
Effects are generally experienced at the organism level	Effects are experienced from organism to ecosystem levels	Effects are usually manifested at the ecosystem level
Objectives are established on the basis of laboratory tests	Objectives are established by laboratory or controlled environmental and field studies	Ecosystem studies are required to establish values
Lethality or physiological effects are the usual response used in setting objectives	Physiological, growth and ecosystem effects are caused by direct or indirect mechanisms	Ecosystem effects are caused by direct (abiotic change) or indirect (biotic interaction) mechanisms
Environmental objectives are set well below known effects to provide some margin of safety	Objectives are set as close to effect thresholds as possible	Objectives are set as close to effect thresholds as possible
No beneficial effects are likely to occur in the environment at any level	Changes may occur that are deemed beneficial (such as increased growth)	Changes may occur that are deemed beneficial (such as increased productivity)
Environmental damage from exceedances is usually observed within a short time	Environmental damage usually results from short- to medium-term exceedances	Environmental damage usually results from long-term (years, decades) exceedances and may be cumulative

ECE to define air pollutant emission control strategies for the whole of Europe. They are being or may be used in a series of protocols relating to the control of sulfur dioxide, nitrogen oxides, total nitrogen (including oxidized and reduced species) and ozone. Full use has been made in this publication of the data that underpin these protocols. The proposed guidelines cover the same range of air pollutants and are aimed at a wide range of vegetation types and ecosystems. Individual species, vegetation types and

ecosystems may vary in their sensitivity to a given pollutant, and this sensitivity may also depend on other factors such as soil type or climate. When possible, therefore, different values of critical loads or levels are defined, depending on the relevant factors. When this approach is not possible, values are based on protecting the most sensitive type of vegetation or ecosystem for which good quality data are available.

There is thus a sound scientific basis for expecting that adverse ecological and economic effects may occur when the guidelines recommended below are exceeded. There is a possibility that adverse effects might also occur at exposures below these guidelines, but there is considerable uncertainty over this and it was decided to recommend values with a sound scientific basis rather than to incorporate arbitrary uncertainty factors. Critical levels and critical loads thus fulfil the primary aim of air quality guidelines in providing the best available sound scientific basis for the protection of vegetation from significant effects.

To carry out an assessment based on the guidelines, due consideration has to be given to the various problems caused by air pollution and their impact on the stock that may be at risk. The requirements for the former are often different from those needed to assess the risks to human health. Nevertheless, methodologies have been developed that can assess the risks of damage to vegetation and ecosystems.

Because of the different definition of critical loads and critical levels, the variable nature of the ecological impacts caused by different pollutants, and the different types of scientific evidence available, it is not possible to use a single methodology to derive the air quality guidelines presented in this section. For critical levels, the methods used rely on analysis either of experimental studies in the laboratory or in field chambers, or of field studies along pollution gradients. For critical loads, the methods used rely on analysis of field experiments, comparisons of sites with different deposition rates, or modelling. Where possible, data from a combination of sources are used to provide the strongest support for the proposed guidelines. Uncertainties in defining guidelines can arise (*a*) because of the limited availability of appropriate data; (*b*) because the data exist only for specific vegetation types and climates and therefore may not be representative of all areas of Europe; or (*c*) because exposure patterns in experimental chambers may not be representative of those under field conditions.

In the field, pollutants are never present in isolation, while the same pollutant may have several impacts simultaneously (for example, exposure to

sulfur dioxide can cause direct effects on leaf physiology and contribute to long-term acidification, while deposition of nitrogen can cause both acidification and eutrophication). Currently, knowledge of the impacts of pollutant combinations is inadequate to define critical loads or levels for such combined impacts, and thus the guidelines are recommended for the ecological effects of individual pollutants. When applying these guidelines in ecological risk assessment, the possibility of such combined impacts should be considered. Furthermore, when considering an area of mixed vegetation types or ecosystems, several guidelines may apply. Thus ecological risk assessment applying the critical levels and loads approach must be aimed at identifying or protecting the most sensitive element of the environment.

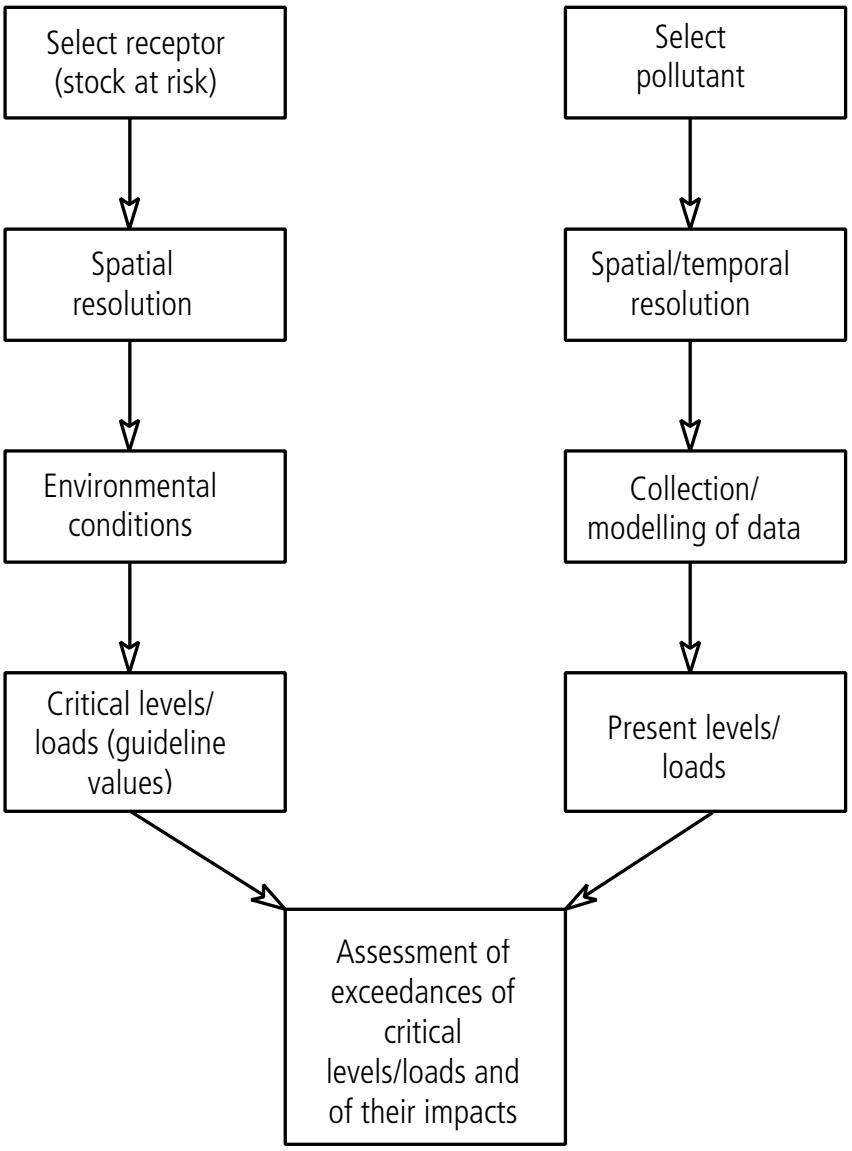
A simple overview of the elements of how critical levels and critical loads can be used is given in Fig. 2. The left- and right-hand pathways indicate the requirements, enabling finally the comparison of critical levels or critical loads with ambient air concentrations (present levels) or pollutant depositions (present loads) on broad spatial scales. The left-hand pathway depicts the steps needed to obtain a geographical distribution of critical levels and loads over European ecosystems.

Since critical levels and critical loads indicate the sensitivity of receptors (such as individual plant species or ecosystems) to air pollutants, an important step in the critical levels/loads application pathway consists of the geographical determination and mapping of the receptors and their sensitivities, at as fine a spatial resolution as possible.

Critical levels are in most cases formulated in such a way that a certain receptor type (such as forests or crops) has the same critical level value throughout Europe. In these cases, the resulting sensitivity maps look uniform over large areas. More recent developments in critical levels research attempt to incorporate environmental conditions into the assessment. The incorporation of such modifying factors – such as water availability, which influences the opening of the stomata and thus the uptake of gaseous pollutants by plants – can lead to a higher degree of differentiation in the mapping of sensitivities.

Critical loads are also allocated to certain receptor types, such as forests, bogs, heathlands, grasslands or lakes, but the spatial differentiation is generally more advanced than in the case of critical levels. It is often possible to take into account environmental conditions such as soil characteristics, water conditions, precipitation amounts, land use and management practices. The result is a critical load map with a high spatial variation in sensitivities.

Fig. 2. Critical levels/loads application pathway



The right-hand pathway in Fig. 2 depicts steps to ensure comparability of present levels/loads with critical levels/loads. The comparison with present ambient air concentrations or present depositions can only be made if the spatial resolution is compatible with the mapped critical levels/loads. The regional distribution of ambient air concentrations and depositions can be modelled to reflect data measured by national and/or international monitoring networks over Europe. Subject to the spatial resolution of these modelled data, comparisons of critical levels/loads with present levels/loads can be made at finer or coarser spatial resolutions. At the European level, present levels/loads are currently modelled for grid cells with a size of 150 km × 150 km or 50 km × 50 km by the ECE Co-operative

Programme for Monitoring and Evaluation of the Long Range Transmission of Air Pollutants in Europe (EMEP). In the case of depositions, compatibility with the mapped critical loads can be achieved by establishing cumulative frequency distributions of the critical loads occurring in the grid cell. A low percentile value (such as 5) of these distributions can be chosen for comparison with the present loads. If, in the framework of effect-orientated pollutant emission reduction strategies, the present levels or loads are reduced to critical levels or a 5-percentile value of the critical loads distribution, respectively, the protection of most sensitive receptors is reliably estimated to be high (for example achieving potential protection of 95% of the ecosystems in a grid cell).

The left- and right-hand pathways of Fig. 2 finally lead to the assessment of exceedances of critical levels/loads. Exceedances of critical levels/loads are interpreted in a qualitative rather than a quantitative manner, in that the probability of damage is considered to be non-zero whenever critical levels/loads are exceeded. Thus, the exceedance of critical levels/loads implies non-sustainable stress, which can lead to damage at any point in time and to an extent depending on the amount of excess pollution. Research is continuing to determine quantitative regional relationships between the actual excess pollution and the expected damage. Exposure–response relationships for sensitive receptors, established in experimental or field studies and modified for prevailing environmental conditions, may tentatively be used to quantify the consequences of excess pollution. However, research results are considered to lack the robustness needed to allow applications to European ecosystems as a whole.

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Effects of sulfur dioxide on vegetation: critical levels

Since the publication of the first edition of the *Air quality guidelines for Europe* in 1987 *(1)*, the relative importance of sulfur dioxide as a phytotoxic pollutant in Europe has diminished to some extent, owing to falling emissions in many areas. In terms of understanding the basic mechanisms of direct injury by sulfur dioxide, and threshold concentrations for adverse effects, advances have been made in demonstrating the significance of very low concentrations on growth and yield and on changing plant sensitivity to other environmental stresses. New work has also provided information that can be utilized to introduce new guidelines for protecting lichens against sulfur dioxide and forests against acid mists.

A number of studies have provided valuable data for several major agricultural crops, based on fumigations, filtrations and transect studies *(2–4)*. These new data confirm the annual guideline value of 30 μg/m^3 as an annual mean concentration (Table 31). However, it is recommended that this value should also not be exceeded as a mean concentration for the winter months (October–March inclusive) in view of the abundant evidence for increased sensitivity of crops growing slowly under winter conditions. It is recommended that the 24-hour air quality guideline for all species be abandoned, in view of further evidence confirming that peak concentrations are not significant compared with the accumulated dose.

A lower air quality guideline of 20 μg/m^3 is now recommended for forests and natural vegetation, as both an annual and winter mean concentration (Table 31). This is based on new evidence of periods of high sensitivity of conifers during needle elongation and the longevity of many of the species concerned as well as their being unmanaged or minimally managed, which renders them more sensitive to pollution stress *(4–6)*.

New data have confirmed concerns over low-temperature stress contributing to greater sulfur dioxide sensitivity in forests. Further justification for modifying the air quality guideline to take account of interactions with low temperature is given by evidence of sulfate mists enhancing frost sensitivity.

Table 31. Guidelines for the effects of sulfur dioxide on vegetation: critical levels

Vegetation category	Guideline ($\mu g/m^3$)	Time period [a]	Constraints
Agricultural crops	30	Annual and winter mean	
Forests and natural vegetation	20	Annual and winter mean	
Forests and natural vegetation	15	Annual and winter mean	Accumulated temperature sum above +5 °C is < 1000 °C·days per year
Lichens	10	Annual mean	
Forests	1.0 sulfate particulate[b]	Annual mean	Where ground level cloud is present ≥ 10% of time

[a] Where annual and winter mean concentrations are indicated, the higher value should be used to define exceedance. Winter is defined as October to March inclusive.

[b] Air quality guideline only applies in areas of oceanic Europe where calcium and magnesium concentrations in cloud or mist are less than the combined ionic concentrations of H^+ and NH_4^+.

A field study of Norway spruce at different altitudes in the Ore Mountains of Czechoslovakia has been used to develop a model, from which the accumulated temperature sum above +5 °C of < 1000 °C·days per year is used as a threshold for lowering mean annual and winter sulfur dioxide concentrations to 15 $\mu g/m^3$ for protecting forests and natural vegetation. This lower concentration is now recommended as a WHO air quality guideline for regions below this threshold temperature sum (Table 31). It should be recognized, however, that this guideline is based on field studies in a region where the temperatures recorded were above those pertaining in some areas of northern Europe, and thus it is possible that in even more extreme environments a lower guideline is required.

The 1987 edition of the guidelines considered only the effects of sulfur dioxide on higher plants. Many sensitive lichen and bryophyte species have disappeared from large areas of Europe with only moderately elevated sulfur dioxide concentrations. Annual mean concentrations of 30 $\mu g/m^3$ are associated with the eradication of the most sensitive lichen taxa. On the

basis of new field studies, it is recommended that an air quality guideline of 10 μg/m^3 annual mean (Table 31) be established for lichens *(7–9)*.

In the 1987 edition, no consideration was given to direct impacts of acid precipitation on above-ground plant organs. It is now recognized that mists can contain solute concentrations up to ten times those of rain, and can thus have a direct impact on vegetation. Since mists and clouds occur most frequently at high altitudes, and are intercepted with particular efficiency by forests, trees are likely to be the most sensitive receptors. Experiments on young trees, backed up by field observations, show significant effects of acid mists on leaf surface structure at pH 3.5, which is equivalent to 150 μmol/l sulfate. Because of the difficulties of measuring sulfate concentrations in cloud water, a guideline has been set based on the equivalent particulate sulfate concentration. A guideline of 1.0 μg/m^3 particulate sulfate as an annual mean is recommended for trees where ground level cloud is present 10% or more of the time (Table 31). This guideline only applies, however, when calcium and magnesium concentrations in cloud do not exceed hydrogen and ammonium ion concentrations, because no data exist to establish a guideline under other conditions. This restriction excludes areas such as the Mediterranean region, eastern Europe and the Alps.

These guidelines do not take into account that sulfur dioxide increases sensitivity to other stresses, with the exception of low temperatures for forests and natural vegetation. Given further knowledge of its effects on stresses such as drought, pathogens and pests, it is possible that the guidelines may require further modification in the future. The 24-hour mean guideline has been abolished, but this is on the basis of knowledge on higher plants. The inclusion of lichens in these new guidelines may warrant future considerations of a short-term guideline for these organisms, if knowledge indicates the necessity for this. The new guideline for acid mists has similarly been set for forests only, and the effects on other receptors may also warrant future attention.

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Effects of nitrogen-containing air pollutants: critical levels

EFFECT EVALUATION

Various forms of nitrogen pollute the air, mainly nitric oxide (NO), nitrogen dioxide (NO_2) and ammonia (NH_3) as dry deposition, and nitrate (NO_3^-) and ammonium (NH_4^+) as wet deposition. Other contributions are from occult deposition (fog, clouds, aerosols), peroxyacetylnitrate (PAN), dinitrogen pentoxide (N_2O_5), nitrous oxide (N_2O) and amines. Since the publication of the *Air quality guidelines for Europe* in 1987 *(1)* there have been significant advances in knowledge of the impacts of nitrogen oxides (NO_x, i.e. NO_2 and NO) and NH_3 on vegetation.

In the present evaluation, attention is mainly paid to direct effects on plants caused by an exposure duration of between one hour and one year. The long-term impact (more than one year) on vegetation and the nitrogen cycle is discussed in Chapter 14, while the contribution of nitrogen-containing air pollutants to soil acidification is evaluated in Chapter 13. The properties of PAN are discussed in Chapter 12. The role of NO_x and N_2O in atmospheric chemistry (formation and depletion of ozone in the troposphere and stratosphere, respectively) and relations with climate change are not considered.

The reason for defining critical levels for NO, NO_2 and NH_3 is the recent evidence from monitoring and mapping that these are the dominant forms of nitrogen deposition in many parts of the world, and that several important effects of these compounds are not covered by the critical loads for nitrogen or acidity.

The critical levels are based on a survey of published evidence of physiological and ecologically important effects on plants *(2–7)*. Biochemical changes have only been used as additional indicators of potentially relevant ecological responses. The current survey has considered that, in an ecological

context, growth stimulation and reduction are both potentially negative responses. For instance, both NO_x and NH_y (i.e. NH_3 and NH_4^+) generally cause an increase in the shoot:root ratio, which may or may not be beneficial.

Responses to nitrogenous pollutants can be further modified and exacerbated by interactions with other environmental factors, including frost, drought and pest organisms. These interactions generally include increased susceptibility to these factors, which may in turn lead to major ecological changes.

The method of estimating critical levels is different for NO_x and NH_3, but both are based on a 95% protection level (neglecting the 5% lowest effective exposures).

GAPS IN KNOWLEDGE

There have been important developments in the use of critical level and critical load approaches for setting air quality guidelines. With regard to the critical levels of nitrogen-containing air pollutants, however, there are several areas where improvements are urgently required.

- The guidelines for the critical levels of NO_x and NH_3 are intended to apply to all classes of vegetation and under all environmental conditions. However, more information is needed to quantify the range of sensitivity.

- The guideline for NH_3 is based on research performed in temperate climates on a limited range of soil types. To a lesser extent this applies to NO_x as well. Caution is required when critical levels are considered for plants in very different conditions, for example in tropical and subtropical zones.

- There is a need to understand further the long-term impacts on growth of changes in biochemical parameters.

- There is growing awareness of the physiological importance of NO, and this is reflected in the new incorporation of this compound in the guideline for NO_x. Comparisons of the phytotoxicity of NO and NO_2 are scarce and still not conclusive with regard to their relative degree of toxicity.

- The relevance of the emission of NH_3 from plants should be investigated in more detail in order to establish its potential importance in nitrogen budgets.

GUIDELINES

Evidence exists that NH_4^+ (and NO_3^-) in rain, clouds and fog can have significant direct effects on vegetation, but current knowledge is still insufficient to arrive at critical levels for those compounds. It is assumed that NO and NO_2 act in an additive manner.

A strong case can be made for the provision of critical levels for short-term exposures. There are insufficient data to provide these levels with confidence at present, but current evidence suggests values of about 75 µg/m^3 for NO_x and 270 µg/m^3 for NH_3 as 24-hour means.

Interactive effects between NO_2 and sulfur dioxide and/or ozone have been reported frequently *(8–13)*. From a review of recent literature, however, it was concluded that the lowest effective levels for NO_2 are approximately equal to those for combination effects (although in general, at concentrations near to its effect threshold, NO_2 causes growth stimulation if it is the only pollutant, while in combination with sulfur dioxide and/or ozone it results in growth inhibition).

Critical levels for a 1-year period are recommended to cover relatively long-term effects. The critical level for NO_x (NO and NO_2, added in ppb and expressed as NO_2 in µg/m^3) is 30 µg/m^3 as an annual mean. The critical level for NH_3 is 8 µg/m^3 as an annual mean.

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Effects of ozone on vegetation: critical levels

EFFECT EVALUATION

The revision of the air quality guidelines for ozone builds on the progress made to define critical levels to protect crops and tree species. Guidelines for other photochemical oxidants, such as peroxyacetylnitrate and hydrogen peroxide, are not recommended because of the low levels of these pollutants observed in Europe, and because data concerning their effects on plants in Europe are very limited. Research in recent years has mainly advanced our understanding of the exposure, uptake and effects of ozone *(1, 2)*.

Ozone concentrations vary widely both in space and in time, and in order to quantitatively relate ozone exposure to effects it is necessary to summarize the concentration pattern during the exposure period in a biologically meaningful way *(3, 4)*. From results of exposure–response studies with open-top chambers, it is concluded that mean concentrations are not appropriate to characterize ozone exposure. This is mainly because (*a*) the effect of ozone results from the cumulative exposure; and (*b*) not all concentrations are equally effective, higher concentrations having greater effects than lower concentrations. Ozone exposure is therefore expressed as the sum of all 1-hour mean concentrations above a cut-off concentration of 40 ppb. It is emphasized that 40 ppb should not be regarded as a lower concentration limit for biological effects, since some biological effects may occur below this value; rather, it is a cut-off concentration used to calculate an exposure index that is strongly related to biological responses, and hence to the degree of risk to sensitive vegetation.

The use of 40 ppb as the cut-off concentration provides good linear relationships between ozone exposure and plant response for a number of species, thus confirming its biological relevance *(5, 6)*. Furthermore, the ozone concentrations found in most areas of Europe, in the absence of photochemical pollution, are in the range 10–40 ppb, except at very high altitudes. In relation to long-term effects, this sum (referred to as the "Accumulated exposure Over a Threshold of 40 ppb", AOT40), is calculated for a 3-month growing season in the case of crops or herbaceous semi-natural

vegetation, or a 6-month growing season for trees. The appropriate months to define the growing season will depend on the vegetation and climate in a specific region or at a specific site. Since uptake of ozone by vegetation occurs primarily during daylight hours when stomata are open, the calculation of the AOT40 considers only those hours when radiation is higher than 50 W/m^2.

To define critical levels, the AOT40 is related to specific effects *(2)*. A reduction in economic yield (such as grain yield in wheat) is considered the most relevant long-term effect of ozone on crop species, and a reduction in biomass is chosen for tree species. For semi-natural vegetation, the effect of ozone is expressed as the change in the species composition. The most important short-term effect of ozone is the appearance of visible leaf injury. The most sensitive species for each vegetation type for which adequate data are available was selected to derive the critical level.

For crops, data on grain yield of spring wheat exposed in open-top field chambers to different ozone concentrations over the growing season were used to set the critical level, since the database is the largest (10 experiments in 6 countries using 10 different cultivars) and most consistent, and wheat is known to be a sensitive species. Statistical analysis of this pooled dataset showed that the least significant deviation in yield that can be estimated with 99% confidence is 4–5%. The critical level determined using this criterion (Table 32) is 3 ppm·h *(5, 7)*.

The critical level for short-term effects of ozone on crops (visible injury) is derived from an extensive database of coordinated European field observations, involving eight countries over two growing seasons using two clover species *(8)*. Using artificial neural network analysis, combinations of ozone exposure and climatic conditions in the five days preceding the onset of visible injury were identified and used to set critical levels (Table 32) of 0.2 ppm·h for humid air conditions (mean vapour pressure deficit below 1.5 kPa) and 0.5 ppm·h for dry air conditions (mean vapour pressure deficit above 1.5 kPa).

For forests, the database available is small. Data sets from three different European studies using open-top field chambers of the effects of ozone on annual biomass increment in beech saplings have been used *(9)*. Statistical analysis of these data showed that the least significant deviation in biomass increment that could be estimated with 95% confidence was about 10%, and this criterion was used to determine a critical level of 10 ppm·h (Table 32).

Table 32. Guidelines for the effects of ozone on vegetation: critical levels

Vegetation type	Guidelines AOT40 (ppm·h)	Time period[a]	Constraints
Crops (yield)	3	3 months	
Crops (visible injury)	0.2	5 days	Humid air conditions (mean daytime VPD[b] below 1.5 kPa)
	0.5	5 days	Dry air conditions (mean daytime VPD[b] above 1.5 kPa)
Forests	10	6 months	
Semi-natural vegetation	3	3 months	

[a] Daylight hours.

[b] VPD = vapour pressure deficit.

Finally, for herbaceous species of semi-natural vegetation, recent studies have reported the effects of ozone in field or laboratory chambers on shoot biomass, seed biomass or relative growth rate of a total of 87 species. All studies showed significant adverse effects, at the 95% confidence level, of exposures in the range 3–5 ppm·h on the most sensitive species studied. Since there is also evidence that the most sensitive of these species are as sensitive as the most sensitive known crop species, a critical level of 3 ppm·h (Table 32), equivalent to that for crops, has been adopted *(10)*.

GUIDELINES

The data used to derive critical levels are almost entirely drawn from experiments in open-top chambers in central and northern Europe, using plants that are adequately supplied with water and nutrients. There are uncertainties in using these data to define air quality guidelines for vegetation throughout Europe. Among the most important of these uncertainties are the following.

- The open-top chamber technique will tend to overestimate the effects because of the higher ozone fluxes within the chambers compared with outside.
- There are a great many species that have not been investigated experimentally in Europe, especially in the Mediterranean region.

- The critical level is likely to be higher when water availability is limited, because ozone flux is reduced. This is a very significant factor in many areas of Europe, especially as periods of water stress often coincide with periods of high ozone concentration.
- There may be physiological, morphological or biochemical changes induced by ozone exposures below the critical level that could be important, for example in altering sensitivity to other abiotic and biotic stresses.
- The data on trees are more variable than those for annual crops and there is uncertainty about the extent and significance of night-time ozone uptake. Furthermore, there are uncertainties in extrapolating from experiments of limited duration with young pot-grown trees to long-term effects on forest ecosystems. For these reasons, there is greater uncertainty attached to the recommended guidelines for trees.
- For changes in species composition, the experiments are also of limited duration, and there is great uncertainty about the long-term effects of ozone exposure.

When determining whether ozone exposures at a specified location exceed the critical levels (Table 32), two points need to be carefully considered.

1. Over short vegetation, but not over forests, there may be significant gradients in AOT40 immediately above the vegetation, and thus AOT40 values determined at the measurement height of most monitoring stations may be larger than at the surface of the vegetation. In contrast, in experimental chambers used to generate the exposure–response data, the air is well mixed and the gradients do not exist.

2. AOT40 values can vary substantially from year to year, because of the variability of the climate. Because the critical level for crop yield was based on analysis of data in several different growing seasons, and because the critical level for forests was based on multi-year experiments, it is recommended that the exceedance of these critical levels, and that for semi-natural vegetation, be evaluated on the basis of mean AOT40 values over a 5-year period. Where visible injury to crops resulting from short-term exposures is of direct economic concern, however, examination of monitoring data for the year with highest ozone exposures is recommended.

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Indirect effects of acidifying compounds on natural systems: critical loads

ACIDIFYING DEPOSITION AND ECOSYSTEM DAMAGE

Historical data provide evidence of increasing transport of sulfate (SO_4^{2-}), up to a factor of 2 and 3.5 in 1950 and 1980, respectively, compared to pre-industrial levels in Europe. Emissions of sulfur dioxide in the air are transformed to sulfate, which constitutes the major compound of acid deposition *(1, 2)*. The effects and risks of sulfur dioxide emissions and resulting deposition are described for soils in general and for forest soils and surface waters in particular.

Soil acidification is defined as a decrease in the acid neutralizing capacity (ANC) of the inorganic fraction of the soil including the solution phase, and is directly dependent on the net supply of base cations (by weathering and deposition) and the net supply of anions (deposition minus retention) in the mineral soil *(3, 4)*. Deposition of acidifying compounds such as sulfur dioxide, nitrogen oxides and ammonia leads to soil acidification by oxidation to sulfuric and nitric acids and leaching of sulfate and nitrate, respectively.

The dynamics of forest soil acidification is very site-specific and depends on soil characteristics such as weathering rate, sulfate adsorption capacity and cation exchange capacity. The acidification of soils ultimately leads to an increase in the soil solution of the aluminium concentration, which increases the risk of vegetation damage. By defining the relationship between the chemical status (base cation and aluminium concentrations in the soil solution) and vegetation response, the so-called critical load for that particular ecosystem can be derived *(5)*. Damage to forests in Europe, including defoliation, discoloration, growth decrease and tree dieback, have been reported over the last decade, and have to a large extent been attributed to soil acidification, but also to eutrophication and photochemical oxidant effects.

Acidic deposition has caused acidification of surface waters, fish mortality and other ecological changes in large areas of northern Europe and eastern parts of North America.

Sulfate is normally a mobile anion in catchments located in glaciated areas. Increased sulfate concentrations in runoff due to increased acidifying inputs are accompanied by an increase of base cations and a decrease in bicarbonates, resulting in an acidifying effect on surface waters.

For most of the sensitive soils in Europe, the sulfate deposition is directly related to the acidifying load of sulfate in watershed runoff. The deposition/runoff relationship for nitrogen is not as well defined. The nitrate concentration in runoff, and hence the contribution to the total acidity loading, is due to a combination of factors including the amount of deposition, the ability of vegetation to take up nitrogen and the denitrifying processes. Even in cases of substantial nitrogen runoff, models calculate a deposition/runoff ratio greater than 1 due to denitrification. Determining the nitrate runoff response to a change in nitrogen deposition requires site-specific information.

Under natural conditions, most of the nitrogen deposited on terrestrial catchments is taken up by vegetation, leading to low concentrations of ammonia and nitrate in the runoff. In some areas in Europe, however, including Denmark, southern Norway and southern Sweden, nitrogen concentrations in runoff water appear to be above background values. This excess nitrate in runoff is mostly due to a disruption of the nitrogen cycle and not only to increased nitrogen deposition. In such cases, nitrogen deposition exceeds the rate of nitrogen retention mechanisms, i.e. growth uptake, denitrification and immobilization. When nitrate is leached from the soil solution and appears in surface waters, it will contribute to soil and surface water acidification in the same manner as sulfate.

In cases of low soil pH, excess nitrogen deposition leads to acidification of natural vegetation systems other than trees. Plant species from poorly buffered habitats are adapted to nitrate uptake, while plants from acid environments are generally adapted to ammonia uptake. A low pH may thus lead to a shift of these systems from a nitrate-dominated to an ammonia-dominated system. Such a disruption of the nitrogen cycle in combination with low pH ultimately leads to acidification by nitrogen.

CRITICAL LOADS

The critical load of acidity means "the highest deposition of compounds that will not cause chemical changes leading to harmful effects on ecosystem structure and function" *(6)*.

A relationship has been established between increased aluminium concentrations in the soil solution and adverse effects to roots and growth of trees. For example, it has been shown that the tree growth of Norway spruce decreases as the base cation (calcium, magnesium, potassium) to aluminium (BC/Al) ratio is smaller than a critical limit of 1 *(7)*. Other critical limits for forest soils are based on aluminium concentration and pH in soil solution. Laboratory results of aluminium damage indicate that tolerance to aluminium varies among tree species. For example, a growth reduction of 80% has been demonstrated at a BC/Al ratio of 0.1 for the northern white cedar (*Thuja occidentalis*) and of 4 for the masson pine (*Pinus massoniana*). It has been found that a BC/Al ratio exceeding or equal to 1 seems to provide appropriate sustainability for European forests. However, species that grow in non-glaciated old soils rich in aluminium oxide, such as teak, guapira, orange and cotton, seem to be more accustomed to aluminium than trees from the temperate zone. Computations of critical loads in Europe have therefore generally applied a BC/Al ratio of 1 *(7)*.

For surface waters, the ANC has been considered a chemical criterion that is used to explain the increased risk of damage to fish populations. The critical chemical value, ANC limit = 20 μeq/l, has been derived from the information on water chemistry and fish status obtained from the 1000-lake survey carried out in Norway in 1986 *(8, 9)*. The selected ANC limit was assessed by examining the relationship between the critical load exceedance, and damage to fish populations on the basis of data from the Norwegian 1000-lake survey can again be used *(10)*. The probability of damage to fish populations increases clearly as a function of the critical load exceedance. Table 33 gives an overview of average limits that have been established to compute critical loads.

Calculation of critical loads is based on the steady state mass balance method which assumes a time-independent steady state of chemical interaction involving an equilibrium between the production and the consumption of acidic compounds.

Current United Nations Economic Commission for Europe (ECE) protocols concentrate on distinctive acidifying compounds, such as sulfur and nitrogen, rather than on acidity as a whole. It was necessary to subdivide

Table 33. Critical limits for chemical compounds and properties in forest soils and freshwater systems

Compound / property	Unit	Forest soil	Fresh water	Groundwater
Aluminium	mol_c/m^3	0.2	0.003	0.02
BC/Al	mol/mol	1	–	–
pH	–	4.0 [a]	(5.3, 6.0)[b]	6.0
ANC	mol_c/m^3	–	(0.02, 0.08)[b]	0.14
NO_3^-	mol_c/m^3	–	–	0.8

[a] Assuming log K_{gibb} of 8.0 and Al = 0.2 mol_c/m^3.

[b] A pH of 6.0 relates to peak flow situations and is associated with ANC = 0.08 mol_c/m^3.

the critical load of acidity between the acidifying share of sulfur and that of nitrogen. For the purposes of the guidelines no subdivisions are performed.

GUIDELINES

In Europe, critical loads have been established at the EMEP resolution (see page 225) to allow for comparisons between critical loads and sulfur deposition values, and to identify areas where critical loads are exceeded. Critical loads of acidity, as computed by the steady state mass balance method, depend predominantly on the rate of base cation weathering. For terrestrial ecosystems, the weathering rate can be estimated by combining information on soil parent material and texture properties. The critical loads of acidity in relation to combinations of parent material and texture classes range from smaller than 250 eq/ha per year to more than 1500 eq/ha per year (see Table 34).

Additional factors, such as vegetation cover, further modify the value of the critical load. To calculate precise critical loads for a given geographical area, it is recommended that the mass balance equation be used. For surface waters, the weathering rate can be estimated on the basis of water quality and quantity variables, of which base cation concentrations and runoff are the most influential ones.

Table 34. Critical load ranges of acidity used for the various combinations of parent material and texture in terrestrial ecosystems

Guideline range of critical loads of acidity (eq/ha per year)	Parent material[a]	Texture[b]
< 250	acidic	coarse
250–500	acidic	coarse-medium
	intermediate	coarse
	basic	coarse
500–1000	acidic	medium, medium-fine
	intermediate	coarse-medium, medium
	basic	coarse-medium
1000–1500	intermediate	medium-fine
	basic	medium
> 1500	intermediate	fine
	basic	medium-fine

[a] Acidic: sand (stone), gravel, granite, quartzine, gneiss (schist, shale, greywacke, glacial till).
Intermediate: gronodiorite, loess, fluvial and marine sediment (schist, shale, greywacke, glacial till).
Basic: gabbro, basalt, dolomite, volcanic deposits.

[b] Coarse: clay content < 18%.
Medium: clay content 18–35%.
Fine: clay content > 35%.

Table 35 lists the ranges of critical loads in relation to combinations of base cation concentration and runoff classes. For each critical load class, at least 50% of the critical load values computed on the basis of lake data from Finland (1450 lakes), Norway and Sweden fall within the class boundaries, given the ranges for present base cation concentrations and runoff. Only in two cases did the boundaries for the base cation concentration classes overlap between two critical load classes, when the class boundaries were set on the basis of the 25th and 75th percentile base cation concentrations for given runoff classes. For those cases the critical loads are determined more by other factors than base cation levels and runoff, and the guideline value set is therefore more uncertain than those without overlap.

Table 35. Critical load ranges of acidity used for various combinations of base cation concentration and runoff for surface waters

Guideline range of critical loads of acidity (eq/ha per year)	Base cation concentration (meq/m^3)	Runoff (m)
< 250	< 45	> 1.0
	< 100	0.3–1.0
	< 270 [a]	< 0.3
250–500	45–70	> 1.0
	100–190	0.3–1.0
	250–400 [a]	< 0.3
500–1000	70–103	> 1.0
	190–290	0.3–1.0
	400–650	< 0.3
1000–1500	103–170	> 1.0
	290–465 [a]	0.3–1.0
	650–1300	< 0.3
> 1500	> 170	> 1.0
	> 350 [a]	0.3–1.0
	> 1300	< 0.3

[a] The class boundaries overlap.

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Effects of airborne nitrogen pollutants on vegetation: critical loads

Most of earth's biodiversity is found in natural and seminatural ecosystems, both in aquatic and terrestrial habitats. Man's activities pose a number of threats to the structure and functioning of these ecosystems, and thus to the natural variety of plant and animal species. One of the major threats in recent years is the increase in airborne nitrogen pollution, namely NH_y (consisting of ammonia and ammonium ions), and NO_x (consisting of nitrogen dioxide and nitric oxide). Nitrogen is the limiting nutrient for plant growth in many of these ecosystems. Most of the plant species from these habitats are adapted to nutrient-poor conditions, and can only compete successfully on soils with low nitrogen levels *(1)*. Nitrogen is the only nutrient whose cycle through the ecosystem is almost exclusively regulated by biological processes.

To establish reliable critical loads for nitrogen, it is essential to understand the effects of nitrogen on these ecosystem processes. The critical loads for nitrogen depend on:

- the type of ecosystem;
- the land use and management in the past and present; and
- the abiotic conditions, especially those that influence the nitrification potential and immobilization rate in the soil.

The impacts of increased nitrogen deposition on biological systems are diverse, but the most important effects are:

- short-term direct effects of nitrogen gases and aerosols on individual species (see Chapter 11);
- soil-mediated effects;
- increased susceptibility to secondary stress factors; and
- changes in (competitive) relationships between species, resulting in loss of biodiversity.

The empirical approach has been used to establish guidelines for excess nitrogen deposition on natural and seminatural vegetation. It was decided not to include the results of the mass balance approach with nitrogen as a nutrient for non-forest ecosystems, because essential data are missing. The acidifying effects of airborne nitrogen are incorporated in the guidelines for excess acidity based on steady state mass balance models (see Chapter 13).

EVALUATION OF CRITICAL LOADS

The main aim of this evaluation was to update the guideline for airborne nitrogen deposition on vegetation, which was estimated at 30 kg/ha per year for sensitive vegetation *(2)*. Since 1987, significant progress has been made in understanding the ecological effects of nitrogen deposition on several types of vegetation. Critical loads of nitrogen have been formulated on an empirical basis by observing changes in the vegetation, fauna and biodiversity *(3, 4)*. Experiments under controlled and field conditions, and comparisons of vegetation and fauna composition in time and space, are used to detect changes in ecosystem structure *(5–7)*.

Changes in plant development and in species composition or dominance have been used as a "detectable change" for the impacts of excess nitrogen deposition, but in some cases a change in ecosystem function, such as nitrogen leaching or nitrogen accumulation, has been used. The results of dynamic ecosystem models, integrating both biotic and abiotic processes, are also used where available. Based on these data, guidelines for nitrogen deposition (critical loads) have been presented for receptor groups of natural and seminatural ecosystems, namely:

- wetlands, bogs and softwater lakes
- species-rich grasslands
- heathlands
- forest ecosystems (including tree health and biodiversity).

Critical loads have been defined within a range per ecosystem, because of (*a*) real intra-ecosystem variation within and between countries, (*b*) the range of experimental treatment where an effect was observed or not observed, or (*c*) uncertainties in deposition values, where critical loads are based on field observations. The reliability of the figures presented is shown in Table 36.

It is advised, where insufficient national data are available, to use the lower, middle or upper part of the ranges of the nitrogen critical loads for terrestrial

Table 36. Guidelines for nitrogen deposition to natural and seminatural freshwater and terrestrial ecosystems

Ecosystem	Critical load [a] (kg N/ha per year)	Indication of exceedance
Wetlands		
Softwater lakes	5–10 [##]	Decline in isoetid aquatic plant species
Ombrotrophic (raised) bogs	5–10 [#]	Decrease in typical mosses; increase in tall graminoids; nitrogen accumulation
Mesotrophic fens	20–35 [#]	Increase in tall graminoids; decline in diversity
Species-rich grasslands		
Calcareous grasslands	15–35 [#]	Increase in tall grasses; decline in diversity [b]
Neutral–acid grasslands	20–30 [#]	Increase in tall grasses; decline in diversity
Montane–subalpine grassland	10–15 [(#)]	Increase in tall graminoids; decline in diversity
Heathlands		
Lowland dry heathland	15–20 [##]	Transition from heather to grass
Lowland wet heathland	17–22 [#]	Transition from heather to grass
Species-rich heaths/acid grassland	10–15 [#]	Decline in sensitive species
Upland *Calluna* heaths	10–20 [(#)]	Decline in heather, mosses and lichens
Arctic and alpine heaths	5–15 [(#)]	Decline in lichens, mosses and evergreen dwarf shrubs; increase in grasses
Trees and forest ecosystems		
Coniferous trees (acidic; low nitrification rate)	10–15 [##]	Nutrient imbalance
Coniferous trees (acidic; moderate–high nitrification rate)	20–30 [#]	Nutrient imbalance

Table 36. (contd)

Ecosystem	Critical load [a] (kg N/ha per year)	Indication of exceedance
Trees and forest ecosystems (contd)		
Deciduous trees	15–20 #	Nutrient imbalance; increased shoot/root ratio
Acidic coniferous forests	7–20 ##	Changes in ground flora and mycorrhizas; increased leaching
Acidic deciduous forests	10–20 #	Changes in ground flora
Calcareous forests	15–20 (#)	Changes in ground flora
Acidic forests (unmanaged)	7–15 (#)	Changes in ground flora and leaching
Forests in humid climates	5–10 (#)	Decline in lichens; increase in free-living algae

[a] ## *Reliable*: a number of published papers on various types of study show comparable results.
Fairly reliable: the results of some studies are comparable.
(#) *Expert judgement*: no data are available for this type of ecosystem; the critical load is based on knowledge of ecosystems likely to be more or less comparable with this ecosystem.

[b] Use low end of the range for nitrogen-limited and high end for phosphorus-limited calcareous grasslands.

receptor groups according to the general relationships between abiotic factors and critical loads for nitrogen (Table 37).

At this moment, the critical loads are set in values of total nitrogen inputs. More information is needed in future on the relative effects of oxidized and reduced nitrogen deposition. Critical loads for nitrogen are formulated as reliably as possible. As most research has focused on acidification in forestry, serious gaps in knowledge exist on the effects of enhanced nitrogen deposition on natural and seminatural terrestrial and aquatic ecosystems. The following gaps in knowledge are particularly important:

- more research is needed in Mediterranean, tropical and subtropical vegetation zones;
- quantified effects of enhanced nitrogen deposition on fauna in all types of vegetation reviewed are extremely scarce;
- the critical loads for nitrogen deposition to Arctic and alpine heathlands and forests are largely speculative;

- more research is needed on the effects of nitrogen on forest ground vegetation and (ground) fauna, because most research had focused on the trees only;
- there is a serious gap in knowledge on the effects of nitrogen on neutral/calcareous forests that are not sensitive to acidification;
- more long-term research is needed in montane/subalpine meadows, species-rich grasslands and ombrotrophic bogs;
- the long-term effects of enhanced atmospheric nitrogen in grassland and heathland of great importance for nature conservation under different management regimes are insufficiently known and may affect the critical load value;
- the possible differential effects of the deposited nitrogen species are insufficiently known for the establishment of critical loads; and
- the long-term effects of nitrogen eutrophication in (sensitive) aquatic ecosystems (freshwater and marine) need further research.

GUIDELINES

To establish reliable guidelines, it is crucial to understand the long-term effects of increased nitrogen deposition on ecological processes in a representative range of ecosystems. It is thus very important to quantify the effects of nitrogen loads on natural and seminatural terrestrial and freshwater ecosystems by manipulation of nitrogen inputs in long-term ecosystem studies in unaffected and affected areas. These data are essential to validate the presented critical loads and to develop robust dynamic ecosystem models reliable enough to calculate critical loads for nitrogen deposition in such ecosystems.

Table 37. Suggestions for using the lower, middle or upper part of the set critical loads of terrestrial ecosystems (excluding wetlands) if national data are insufficient

Action	Temperature	Soil wetness	Frost period	Base cation availability
Move to lower part	Cold	Dry	Long	Low
Use middle part	Intermediate	Normal	Short	Intermediate
Move to higher part	Hot	Wet	None	High

Guidelines for nitrogen deposition to natural and seminatural ecosystems are given in Table 36. The most sensitive ecosystems have critical loads of 5–10 kg N/ha per year. An average value for natural and seminatural ecosystems is 15–20 kg N/ha per year.

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ANNEX I

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BARCELONA, SPAIN, 12–14 MAY 1997

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WHO published the first edition of these guidelines in 1987. Since then new data have emerged and new developments in risk assessment methodology have taken place, necessitating the updating and revision of the existing guidelines. The Bilthoven Division of the WHO European Centre for Environment and Health has undertaken this process in close cooperation with the International Programme on Chemical Safety and the European Commission.

It is the aim of the guidelines to provide a basis for protecting public health from adverse effects of air pollutants and to eliminate or reduce exposure to those pollutants that are known or likely to be hazardous to human health or wellbeing. The guidelines are intended to provide background information and guidance to international, national and local authorities in making risk assessment and risk management decisions. In establishing pollutant levels below which exposure – for life or for a given period of time – does not constitute a significant public health risk, the guidelines provide a basis for setting standards or limit values for air pollutants.

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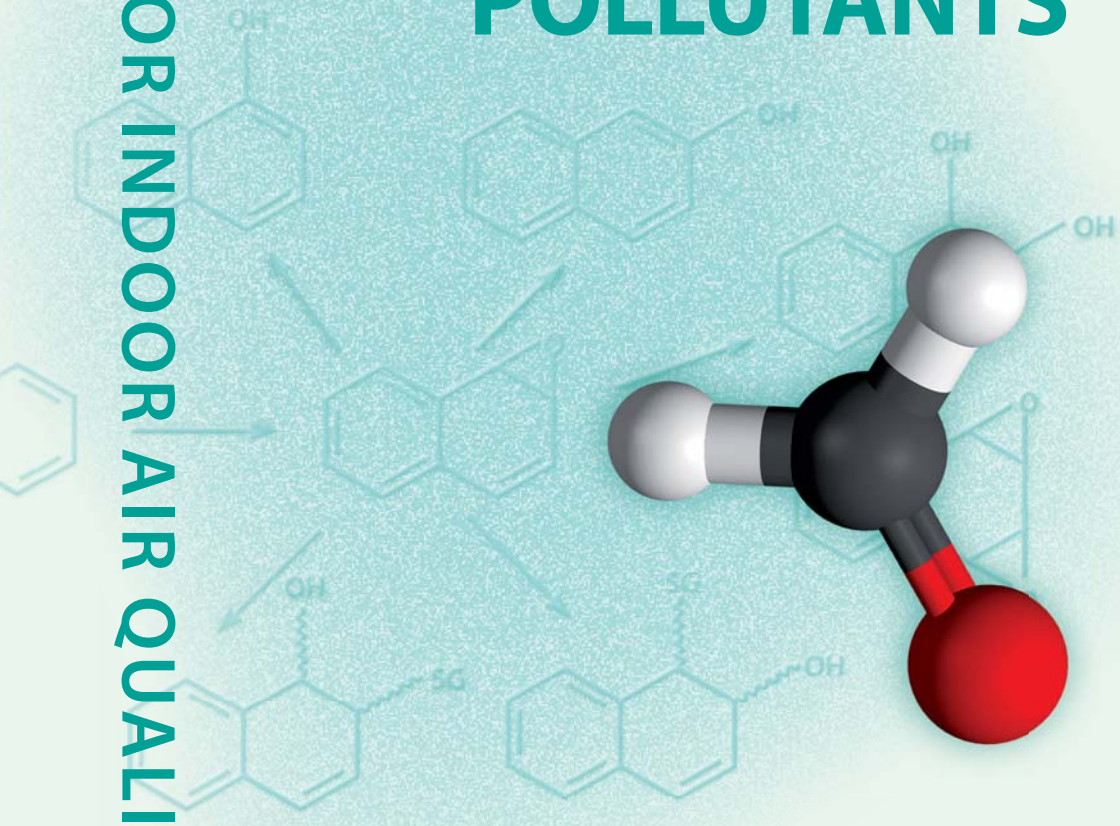
WHO GUIDELINES FOR INDOOR AIR QUALITY

SELECTED POLLUTANTS



WHO guidelines for indoor air quality: selected pollutants

The WHO European Centre for Environment and Health, Bonn Office,
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WHO guidelines for indoor air quality: selected pollutants

Abstract

This book presents WHO guidelines for the protection of public health from risks due to a number of chemicals commonly present in indoor air. The substances considered in this review, i.e. benzene, carbon monoxide, formaldehyde, naphthalene, nitrogen dioxide, polycyclic aromatic hydrocarbons (especially benzo[*a*]pyrene), radon, trichloroethylene and tetrachloroethylene, have indoor sources, are known in respect of their hazardousness to health and are often found indoors in concentrations of health concern. The guidelines are targeted at public health professionals involved in preventing health risks of environmental exposures, as well as specialists and authorities involved in the design and use of buildings, indoor materials and products. They provide a scientific basis for legally enforceable standards.

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Declaration of interests

A standard "Declaration of interests for WHO experts" form was completed by all experts involved in the preparation of the guidelines. Twenty-six experts declared an interest in the subject matter of the meetings/guidelines. All responses were reviewed by the WHO Legal Office and Guidelines Review Committee. The declared interests are listed below.

Potential interests judged by WHO as being insignificant for the guidelines process: experts cleared to participate in the development of the guidelines

Vernon Benignus reported having received remuneration for employment and consultancy from a commercial entity or other organization with an interest related to the subject of air pollution. He also reported having provided an expert opinion or testimony for a commercial entity or other organization as part of a regulatory, legislative or judicial process. He equally stated having held an office or other position, paid or unpaid, where he was expected to represent interests or defend a position related to the subject of air pollution.

Juana M. Delgado Saborit and ***Frank Kelly*** reported them or their research unit having received support for research from an organization that is mainly funded by a commercial entity with a major interest related to air pollution. The organization clarified that its research and reporting are independent, regardless of whether its funding is public or private.

Peter Farmer reported having received remuneration for consultancy from a commercial entity or other organization with an interest related to the subject of air pollution.

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Paul Harrison reported him or his research unit having received support for research from a commercial entity or other organization with an interest related to air pollution. He also reported having provided an expert opinion or testimony for a commercial entity or other organization as part of a regulatory, legislative or judicial process related to the subject of air pollution.

Roy Harrison reported a research contract with and funded travel to annual meetings of a research organization active in the field of health effects of air pollution, which receives funding from the motor vehicle industry and other private organizations.

Rogene Henderson reported having been employed by and having given consultation to a commercial entity or other organization with an interest related to the subject of air pollution. She also reported having provided expert opinion or testimony related to the subject of air pollution for a commercial entity or other organization, as well has having held an office or other position, paid or unpaid, where she may have been expected to represent interests or defend a position related to the subject of air pollution.

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David G. Penney has given numerous testimonies on safe levels of carbon monoxide. The potential interest was judged by WHO as being insignificant for the guidelines process.

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Experts excluded from the development of the guidelines

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Foreword

Clean air is a basic requirement of life. The quality of air inside homes, offices, schools, day care centres, public buildings, health care facilities or other private and public buildings where people spend a large part of their life is an essential determinant of healthy life and people's well-being. Hazardous substances emitted from buildings, construction materials and indoor equipment or due to human activities indoors, such as combustion of fuels for cooking or heating, lead to a broad range of health problems and may even be fatal.

Indoor exposure to air pollutants causes very significant damage to health globally – especially in developing countries. The chemicals reviewed in this volume are common indoor air pollutants in all regions of the world. Despite this, public health awareness on indoor air pollution has lagged behind that on outdoor air pollution. The current series of indoor air quality guidelines, focuses specifically on this problem. This volume, the second in the series following that addressing the hazards of dampness and mould, sets guidelines for a range of chemical substances most commonly polluting indoor air. Understanding of the hazards of these substances is a first step in identifying the actions necessary to avoid and reduce the adverse impacts of these pollutants on health. If these guidelines are sensibly applied as part of policy development, indoor exposure to air pollutants should decline and a significant reduction in adverse effects on health should follow.

WHO has a long tradition in synthesizing the evidence on health aspects of air quality and in preparing air quality guidelines defining conditions for healthy air. We are grateful to the outstanding scientists conducting this work. We hope that these new guidelines will be useful globally to people assessing indoor air quality with a view to predicting its effects on health, and also to those with responsibility for introducing measures to reduce health risks from indoor exposure to air pollutants. Prevention of the health effects of poor indoor air quality is needed in all regions of the world, and especially in developing countries. WHO will assist its Member States in implementing the guidelines, synthesizing the evidence on the most effective approaches to indoor air quality management and on the health benefits of these actions. It will continue encouraging the relevant policy developments and intersectoral collaboration necessary for ensuring access to healthy indoor air for everyone.

Zsuzsanna Jakab
WHO Regional Director for Europe

Executive summary

This document presents WHO guidelines for the protection of public health from health risks due to a number of chemicals commonly present in indoor air. The guidelines are based on a comprehensive review and evaluation of the accumulated scientific evidence by a multidisciplinary group of experts studying the toxic properties and health effects of these pollutants.

The substances considered in this review (benzene, carbon monoxide, formaldehyde, naphthalene, nitrogen dioxide, polycyclic aromatic hydrocarbons (especially benzo[*a*]pyrene), radon, trichloroethylene and tetrachloroethylene) have been added to the guidelines considering information on the existence of indoor sources, on the availability of toxicological and epidemiological data and on exposure levels causing health concerns.

Problems of indoor air quality are recognized as important risk factors for human health in both low- and middle- and high-income countries. Indoor air is also important because people spend a substantial proportion of their time in buildings. In residences, day-care centres, retirement homes and other special environments, indoor air pollution affects population groups that are particularly vulnerable owing to their health status or age.

The primary aim of these guidelines is to provide a uniform basis for the protection of public health from adverse effects of indoor exposure to air pollution, and to eliminate or reduce to a minimum exposure to those pollutants that are known or are likely to be hazardous.

The guidelines are targeted at public health professionals involved in preventing health risks of environmental exposures as well as specialists and authorities involved in the design and use of buildings, indoor materials and products. The guidelines are based on the accumulated scientific knowledge available at the time of their development. They have the character of recommendations. Nevertheless, countries may wish to use the guidelines as a scientific basis for legally enforceable standards.

The evidence review supporting the guidelines for each of the selected pollutants includes an evaluation of indoor sources, current indoor concentrations and their relationship with outdoor levels, as well as a summary of the evidence on the kinetics and metabolism and health effects. Based on the accumulated evidence, the experts formulated health risk evaluations and agreed on the guidelines for each of the pollutants as summarized below.

Benzene

Guidelines on exposure levels for indoor air are needed because indoor air is a significant source of benzene exposure and inhalation is the main pathway of

human exposure to benzene. Benzene is present in both outdoor and indoor air. However, indoor concentrations are generally higher than those in outdoor air owing to the infiltration of benzene present in outdoor air and to the existence of many other indoor sources. Typically, indoor concentrations are below the lowest levels showing evidence of adverse health effects. Considering that benzene is present indoors and taking into account personal exposure patterns, which are predominantly indoors, indoor guidelines for exposure are needed.

Benzene is a genotoxic carcinogen in humans and no safe level of exposure can be recommended. The risk of toxicity from inhaled benzene would be the same whether the exposure were indoors or outdoors. Thus there is no reason that the guidelines for indoor air should differ from ambient air guidelines. It is also recommended continuing to use the same unit risk factors. The geometric mean of the range of the estimates of the excess lifetime risk of leukaemia at an air concentration of 1 μg/m^3 is 6×10^{-6}. The concentrations of airborne benzene associated with an excess lifetime risk of 1/10 000, 1/100 000 and 1/1000 000 are 17, 1.7 and 0.17 μg/m^3, respectively.

As noted above, there is no known exposure threshold for the risks of benzene exposure. Therefore, from a practical standpoint, it is expedient to reduce indoor exposure levels to as low as possible. This will require reducing or eliminating human activities that release benzene, such as smoking tobacco, using solvents for hobbies or cleaning, or using building materials that off-gas benzene.

Adequate ventilation methods will depend on the site of the building. In modern buildings located near heavy traffic or other major outdoor sources of benzene, inlets for fresh air should be located at the least polluted side of the building.

Carbon monoxide

Exposure to carbon monoxide reduces maximum exercise ability in healthy young individuals and reduces the time to angina and, in some cases, the time to ST-segment depression in people with cardiovascular disease, albeit at a concentration that is lower than that needed to reduce exercise ability in healthy individuals.

The relationship of carbon monoxide exposure and the carboxyhaemoglobin (COHb) concentration in blood can be modelled using the differential Coburn-Forster-Kane equation, which provides a good approximation to the COHb concentration at a steady level of inhaled, exogenous carbon monoxide. Based on laboratory studies of reduction in exercise capacity in both healthy individuals and volunteers with cardiovascular disease, it was determined that COHb levels should not exceed 2%. The Coburn-Forster-Kane equation is used below to determine the levels of carbon monoxide to which a normal adult under resting conditions for various intervals can be exposed without exceeding a COHb level of 2%.

The previous WHO guidelines were established for 15 minutes to protect against short-term peak exposures that might occur from, for example, an unvented stove; for 1 hour to protect against excess exposure from, for example, faulty appliances; and for 8 hours (which is relevant to occupational exposures and has been used as an averaging time for ambient exposures). We do not recommend changing the existing guidelines.

However, chronic carbon monoxide exposure appears different from acute exposure in several important respects. The latest studies available in 2009, especially those epidemiological studies using very large databases and thus producing extremely high-resolution findings, suggest that the appropriate guideline level for longer-term average concentration of carbon monoxide in order to minimize health effects must be positioned below the 8-hour guideline of 10 mg/m^3. Thus, a separate guideline is recommended to address 24-hour exposures.

Therefore, a series of guidelines relevant to typical indoor exposures is recommended as follows: 100 mg/m^3 for 15 minutes and 35 mg/m^3 for 1 hour (assuming light exercise and that such exposure levels do not occur more often than one per day); 10 mg/m^3 for 8 hours (arithmetic mean concentration, light to moderate exercise); and 7 mg/m^3 for 24 hours (arithmetic mean concentration, assuming that the exposure occurs when the people are awake and alert but not exercising).

Formaldehyde

An indoor air guideline for formaldehyde is appropriate because indoor exposures are the dominant contributor to personal exposures through inhalation and indoor concentrations may be high enough to cause adverse health effects.

The lowest concentration reported to cause sensory irritation of the eyes in humans is 0.36 mg/m^3 for four hours. Increases in eye blink frequency and conjunctival redness appear at 0.6 mg/m^3, which is considered equal to the no observed adverse effect level (NOAEL). There is no indication of accumulation of effects over time with prolonged exposure.

The perception of odour may result in some individuals reporting subjective sensory irritation, and individuals may perceive formaldehyde at concentrations below 0.1 mg/m^3. However, this is not considered to be an adverse health effect. The NOAEL of 0.6 mg/m^3 for the eye blink response is adjusted using an assessment factor of 5 derived from the standard deviation of nasal pungency (sensory irritation) thresholds, leading to a value of 0.12 mg/m^3, which has been rounded down to 0.1 mg/m^3. Neither increased sensitivity nor sensitization is considered plausible at such indoor concentrations in adults and children. This value is thus considered valid for short-term (30-minute) duration, and this threshold should not be exceeded at any 30-minute interval during a day.

Thus, a short-term (30-minute) guideline of 0.1 mg/m^3 is recommended as preventing sensory irritation in the general population.

Evaluations of long-term effects, including cancer, based on a NOAEL and assessment factor approach, as well as estimates from the biologically motivated models, yield similar results, with values of approximately 0.2 mg/m^3. These values are above the guideline for short-term effects of 0.1 mg/m^3. Thus the use of the short-term (30-minute) guideline of 0.1 mg/m^3 will also prevent long-term health effects, including cancer.

The use of low-emitting building materials and products, and preventing exposures to environmental tobacco smoke and other combustion emissions, will minimize exposure-related risk. In addition, ventilation can reduce indoor exposure to formaldehyde.

Naphthalene

The principal health concerns of exposure to naphthalene are respiratory tract lesions, including tumours in the upper respiratory tract demonstrated in animal studies and haemolytic anaemia in humans.

Lesions in the nasal olfactory and, at higher concentrations, also in the respiratory epithelia of rats appear to be the critical non-neoplastic effect. At concentrations about 100-fold higher than the lowest lesion level, severe inflammation and tumours have been reported to occur at these sites.

Increased cell proliferation due to cytotoxicity (cell damage) is considered a key element in the development of airway tumours. The likely involvement of cytotoxic metabolites in the carcinogenic response and the apparent primary non-genotoxicity of naphthalene favour the assumption of the existence of a threshold.

Therefore, the use of a lowest observed adverse effect level (LOAEL)/NOAEL as a threshold, combined with safety factors, is considered to be an appropriate approach for setting indoor air guidelines to minimize the carcinogenic risk to the respiratory tract of naphthalene exposure.

Associated with repeated inhalation exposure of 6 hours per day, 5 days a week for 104 weeks, severe effects in terms of inflammation were observed in almost all rats exposed to the lowest (but still relatively high) naphthalene dose of 53 mg/m^3. In the absence of adequately published data in relation to less severe effects, this can be taken as a LOAEL, even though it is related to severe effects.

Taking this LOAEL as a starting point and adjusting for continuous exposure (dividing by a factor of 24/6 and 7/5), a value of about 10 mg/m^3 is obtained. Further, incorporating a factor of 10 for using a LOAEL rather than a NOAEL, a factor of 10 for inter-species variation and a factor of 10 for inter-individual variation, a guideline value of 0.01 mg/m^3 is established. This guideline value should be applied as an annual average.

Extensive use or misuse of naphthalene mothballs may lead to haemolytic anaemia. Knowledge of the impact of exposure to naphthalene on the risk of haemolytic anaemia in susceptible individuals (glucose 6-phosphate dehydroge-

nase deficiency) cannot be used to define a guideline owing to the lack of adequate exposure data.

In the absence of mothballs or other sources such as combustion of biomass, indoor air concentrations of naphthalene are just above the typical limit of detection of about 0.001 mg/m^3. Since the concentration of naphthalene in the residential environment increases up to 100-fold when mothballs are used, the most efficient way to prevent high exposures would be to abandon (ban) the use of naphthalene-containing mothballs.

Nitrogen dioxide

A 1-hour indoor nitrogen dioxide guideline of 200 μg/m^3, consistent with the existing WHO air quality guideline, is recommended.

At about twice this level, asthmatics exhibit small pulmonary function decrements. Those who are sensitized may have small changes in airway responsiveness to a variety of stimuli already at this level. Studies of the indoor environment provide no evidence for an indoor guideline different to the ambient guideline.

An annual average indoor nitrogen dioxide guideline of 40 μg/m^3, consistent with the existing WHO air quality guideline, is recommended.

The ambient annual average guideline of 40 μg/m^3 was initially based on a meta-analysis of indoor studies. It was assumed that having a gas stove was equivalent to an increased average indoor level of 28 μg/m^3 compared to homes with electric stoves, and the meta-analysis showed that an increase in indoor nitrogen dioxide of 28 μg/m^3 was associated with a 20% increased risk of lower respiratory illness in children.

Homes with no indoor sources were estimated to have an average level of 15 μg/m^3. Several exhaustive reviews to further develop ambient guidelines have not challenged these findings.

Recent well-conducted epidemiological studies that have used measured indoor nitrogen dioxide levels support the occurrence of respiratory health effects at the level of the guideline.

Polycyclic aromatic hydrocarbons

Some polycyclic aromatic hydrocarbons (PAHs) are potent carcinogens and, in air, are typically attached to particles. The primary exposure to carcinogenic PAHs found in air occurs via inhalation of particles. PAHs occur in indoor air as complex mixtures, the composition of which may vary from site to site. Experimental data on metabolism, gene expression and DNA adducts suggest that interactions between PAHs in mixtures may be complex and highly unpredictable for various PAH compositions (inhibitory, additive, synergistic).

In view of the difficulties in developing guidelines for PAH mixtures, benzo[*a*]pyrene (B[*a*]P) was considered to represent the best single indicator compound. Its toxicology is best known, most single PAH concentration data in ambient and

indoor air are for B[*a*]P, and B[*a*]P has widely been used as an indicator compound for exposure in epidemiological studies.

The health evaluation data suggest that lung cancer is the most serious health risk from exposure to PAHs in indoor air. B[*a*]P is one of the most potent carcinogens among the known PAHs.

In its evaluation of PAHs as ambient air pollutants in 2000, WHO expressed a unit cancer risk as a function of the concentration of B[*a*]P taken as a marker of the PAH mixture. Use of the same unit risk factor for indoor air implies that B[*a*]P represents the same proportion of carcinogenic activity of the PAH mixture as in the occupational exposure used to derive the unit risk. This assumption will not always hold, but the associated uncertainties in risk estimates are unlikely to be large.

Reducing exposure to B[*a*]P may also decrease the risk of other adverse health effects associated with PAHs.

Based on epidemiological data from studies on coke-oven workers, a unit risk for lung cancer for PAH mixtures is estimated to be 8.7×10^{-5} per ng/m^3 of B[*a*]P. This is the guideline for PAH in indoor air. The corresponding concentrations for lifetime exposure to B[*a*]P producing excess lifetime cancer risks of 1/10 000, 1/100 000 and 1/1 000 000 are approximately 1.2, 0.12 and 0.012 ng/m^3, respectively.

Radon

Radon is classified by the International Agency for Research on Cancer as a human carcinogen (Group I). There is direct evidence from residential epidemiological studies of the lung cancer risk from radon. The exposure–response relationship is best described as being linear, without a threshold. The excess relative risk, based on long-term (30-year) average radon exposure is about 16% per increase of 100 Bq/m^3, and on this relative scale does not vary appreciably between current smokers, ex-smokers and lifelong non-smokers. Therefore, as the absolute risk of lung cancer at any given radon concentration is much higher in current smokers than in lifelong non-smokers, the absolute risk of lung cancer due to radon is appreciably higher for current and ex-smokers than for lifelong non-smokers. For ex-smokers, the absolute risks will be between those for lifelong non-smokers and current smokers.

The cumulative risk of death from radon-induced lung cancer was calculated for lifelong non-smokers and for current smokers (15–24 cigarettes per day). The derived excess lifetime risks (by the age of 75 years) are 0.6×10^{-5} per Bq/m^3 and 15×10^{-5} per Bq/m^3, respectively. Among ex-smokers, the risk is intermediate, depending on the time since smoking cessation. The radon concentration associated with an excess lifetime risk of 1 per 100 and 1 per 1000 are 67 Bq/m^3 and 6.7 Bq/m^3 for current smokers and 1670 Bq/m^3 and 167 Bq/m^3 for lifelong non-smokers, respectively.

As part of the management of the radon problem, the WHO International Radon Project has recommended that there should be a reference level as an essential tool in this process.[1]

> A national Reference Level does not specify a rigid boundary between safety and danger, but defines a level of risk from indoor radon that a country considers to be too high if it continues unchecked into the future. However, protective measures may also be appropriate below this level to ensure radon concentrations in homes are well below that level. In view of the latest scientific data, WHO proposes a Reference Level of 100 Bq/m^3 to minimize health hazards due to indoor radon exposure. However, if this level cannot be reached under the prevailing country-specific conditions, the chosen Reference Level should not exceed 300 Bq/m^3 which represents approximately 10 mSv per year according to recent calculations by the International Commission on Radiation Protection.

A guide for radon management should include, in addition to the setting of a reference level, building codes, measurement protocols and other relevant components of a national radon programme.

Trichloroethylene

The existence of both positive and negative results has in the past led risk assessors to different interpretations of trichloroethylene (TCE) toxicity and to divergent estimates of human cancer risk. For a health risk evaluation, bearing in mind recent data on a mechanism of action that is not species-specific, the evidence for weak genotoxicity, and the consistency between certain cancers observed in animals and in humans (in particular liver cancer), it is prudent to consider that the carcinogenicity in animals, the positive epidemiological studies and the plausibility of a human cancer risk leads to the recommendation of a non-threshold approach with a risk estimate rather than a safe level.

Therefore, carcinogenicity (with the assumption of genotoxicity) is selected as the end-point for setting the guideline value. The unit risk estimate of 4.3×10^{-7} $(\mu g/m^3)^{-1}$, derived on the basis of increased Leydig cell tumours (testicular tumours) in rats, is proposed as the indoor air quality guideline. This was also the conclusion of WHO in 2000, the European Union in 2004 and the French Agency for Environmental and Occupational Health in 2009.

The concentrations of airborne TCE associated with an excess lifetime cancer risk of 1/10 000, 1/100 000 and 1/1 000 000 are respectively 230, 23 and 2.3 $\mu g/m^3$.

Tetrachloroethylene

Carcinogenicity is not selected as the end-point for setting the guideline value for tetrachloroethylene, for three reasons: the epidemiological evidence is equiv-

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[1] *WHO handbook on indoor radon: a public health perspective*. Geneva, World Health Organization, 2009.

ocal, the animal tumours detected are not considered relevant to humans, and there are no indications that tetrachloroethylene is genotoxic. The derivation of a guideline value is at present based on two non-neoplastic effects as the critical end-point: impaired neurobehavioural performance and early renal changes.

On the basis of a long-term LOAEL for kidney effects of 102 mg/m^3 in dry cleaning workers, a guideline value of 0.25 mg/m^3 has been calculated. In deriving this guideline value, the LOAEL is converted to continuous exposure (dividing by a factor of 4.2 (168/40)) and divided by an uncertainty factor of 100 (10 for use of an LOAEL and 10 for intra-species variation). Recognizing that some uncertainty in the LOAEL exists because the effects observed at this level are not clear-cut and because of fluctuations in exposure levels, an alternative calculation was made based on the LOAEL in mice of 680 mg/m^3 and using an appropriate uncertainty factor of 1000. This calculation yields a guideline value of 0.68 mg/m^3.

A chronic inhalation minimal risk level (MRL) of 0.28 mg/m^3 (0.04 ppm) has been derived by the Agency for Toxic Substances and Disease Registry based on the LOAEL of 15 ppm. The MRL was calculated from this concentration by expanding to continuous exposure (8/24 hours, 5/7 days) and dividing by an uncertainty factor of 100 (10 for use of a LOAEL and 10 for human variability). This reference found significantly prolonged reaction times in workers occupationally exposed to an average of 15 ppm for about 10 years.

The value and appropriateness of establishing a short-term guideline value is questionable because acute effects occur only at very high concentrations of 50 ppm (340 mg/m^3) and higher, compared to generally observed levels in close proximity to dry cleaning facilities. Establishing a long-term value is more protective of human health.

On the basis of the overall health risk evaluation, the recommended guideline for year-long exposure is 0.25 mg/m^3. This is the same as the previous WHO guideline.

Summary table

A synthesis of the guidelines for all pollutants considered in this volume is presented in Table A overleaf.

Table A. Summary of indoor air quality guidelines for selected pollutants

Pollutant	Critical outcome(s) for guideline definition
Benzene	• Acute myeloid leukaemia (sufficient evidence on causality) • Genotoxicity
Carbon monoxide	Acute exposure-related reduction of exercise tolerance and increase in symptoms of ischaemic heart disease (e.g. ST-segment changes)
Formaldehyde	Sensory irritation
Naphthalene	Respiratory tract lesions leading to inflammation and malignancy in animal studies
Nitrogen dioxide	Respiratory symptoms, bronchoconstriction, increased bronchial reactivity, airway inflammation and decreases in immune defence, leading to increased susceptibility to respiratory infection
Polycyclic aromatic hydrocarbons	Lung cancer
Radon	Lung cancer Suggestive evidence of an association with other cancers, in particular leukaemia and cancers of the extrathoracic airways
Trichloroethylene	Carcinogenicity (liver, kidney, bile duct and non-Hodgkin's lymphoma), with the assumption of genotoxicity
Tetrachloroethylene	Effects in the kidney indicative of early renal disease and impaired performance

Guidelines	Comments
• No safe level of exposure can be recommended • Unit risk of leukaemia per 1 µg/m^3 air concentration is 6×10^{-6} • The concentrations of airborne benzene associated with an excess lifetime risk of 1/10 000, 1/100 000 and 1/1 000 000 are 17, 1.7 and 0.17 µg/m^3, respectively	
• 15 minutes – 100 mg/m^3 • 1 hour – 35 mg/m^3 • 8 hours – 10 mg/m^3 • 24 hours – 7 mg/m^3	
0.1 mg/m^3 – 30-minute average	The guideline (valid for any 30-minute period) will also prevent effects on lung function as well as nasopharyngeal cancer and myeloid leukaemia
0.01 mg/m^3 – annual average	The long-term guideline is also assumed to prevent potential malignant effects in the airways
• 200 µg/m^3 – 1 hour average • 40 µg/m^3 – annual average	No evidence for exposure threshold from epidemiological studies
• No threshold can be determined and all indoor exposures are considered relevant to health • Unit risk for lung cancer for PAH mixtures is estimated to be 8.7×10^{-5} per ng/m^3 of B[*a*]P • The corresponding concentrations for lifetime exposure to B[*a*]P producing excess lifetime cancer risks of 1/10 000, 1/100 000 and 1/1 000 000 are approximately 1.2, 0.12 and 0.012 ng/m^3, respectively	B[*a*]P is taken as a marker of the PAH mixture
• The excess lifetime risk of death from radon-induced lung cancer (by the age of 75 years) is estimated to be 0.6×10^{-5} per Bq/m^3 for lifelong non-smokers and 15×10^{-5} per Bq/m^3 for current smokers (15–24 cigarettes per day); among ex-smokers, the risk is intermediate, depending on time since smoking cessation • The radon concentrations associated with an excess lifetime risk of 1/100 and 1/1000 are 67 and 6.7 Bq/m^3 for current smokers and 1670 and 167 Bq/m^3 for lifelong non-smokers, respectively	WHO guidelines provide a comprehensive approach to the management of health risk related to radon
• Unit risk estimate of 4.3×10^{-7} per µg/m^3 • The concentrations of airborne trichloroethylene associated with an excess lifetime cancer risk of 1:10 000, 1:100 000 and 1:1 000 000 are 230, 23 and 2.3 µg/m^3, respectively	
0.25 mg/m^3 – annual average	Carcinogenicity is not used as an end-point as there are no indications that tetrachloroethylene is genotoxic and there is uncertainty about the epidemiological evidence and the relevance to humans of the animal carcinogenicity data

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Introduction

Human beings need a regular supply of food and water and an essentially continuous supply of air. The requirements for air and water are relatively constant (10–20 m^3 and 1–2 litres per day, respectively). That all people should have free access to air and water of acceptable quality is a fundamental human right. Recognizing the need of humans for clean air, in 1987 the WHO Regional Office for Europe published the first edition of *Air quality guidelines for Europe (1)*, containing health risk assessments of 28 chemical air contaminants.

In 2000, WHO published a second edition of the guidelines *(2)* and a "global update" was published in 2006 *(3)*. The second edition focused on the pollutants considered in the first edition. The global update focused on a small group of pollutants (particulate matter, ozone, nitrogen dioxide and sulfur dioxide) but also included chapters that addressed some health-related general subjects of importance to the air pollution field, including a chapter on indoor air quality. The WHO air quality guidelines have played an important role in providing information and guidance for regulatory authorities working in the air pollution field. In Europe, the guidelines are now seen as the key source on which the European Commission's directive on air quality is based.

That people are exposed to air pollutants both outdoors and indoors is obvious. Globally, people are spending an increasing amount of time indoors. There they are exposed to pollutants generated outdoors that penetrate to the indoor environment and also to pollutants produced indoors, for example as a result of space heating, cooking and other indoor activities, or emitted from products used indoors.

The first edition of the *Air quality guidelines for Europe* published in 1987 *(1)* included a chapter on radon and an annex on tobacco smoke, indoor air pollutants with significant adverse public health impacts. The second edition published in 2000 *(2)* provided a section on indoor air pollutants and added man-made vitreous fibres to radon and tobacco smoke.

The 2005 global update of the air quality guidelines *(3)* drew attention to the large impact on health of indoor air pollution in developing countries. The high concentration of particulates and gases found indoors in houses using solid fuel, including biomass, were noted and it was estimated that exposure might be responsible for nearly 1.6 million excess deaths annually and about 3% of the global

burden of disease. This is a huge impact on health; indeed, far larger than that imposed by exposure to outdoor air pollutants.

Work on assessing the health effects of indoor air pollution has lagged behind that on outdoor air pollution for a number of reasons, including:

- the fact that policy development in the air pollution field has focused on outdoor air pollution as a result of the correctly perceived need to deal with the high levels of outdoor air pollutants associated with both coal smoke and photochemical smog;
- the ready applicability of standards to outdoor concentrations of air pollutants;
- the feasibility of monitoring concentrations of outdoor air pollutants on a large scale;
- the focus of epidemiologists on defining coefficients linking outdoor concentrations of air pollutants with effects on health; and
- the fact that the science and policy communities have focused on the public health impacts of air pollution in wealthy developed countries, while often disregarding the larger burden of disease due to indoor air pollution from solid fuel burning in the developing world.

Questions such as: "how could air quality standards be enforced indoors?" have delayed work on specific indoor air quality guidelines. However, WHO has not ignored the problem of indoor exposure to air pollutants and has stressed since the publication of the first edition of the guidelines in 1987 *(1)* that they should be applicable to both indoor and outdoor air. This was reinforced in the global update published in 2006 *(3)* and the guidelines were recommended for application in all microenvironments. It should be noted that the workplace has been specifically excluded: WHO air quality guidelines have not been seen as a basis for occupational exposure standards.

Developing indoor air quality guidelines

Acknowledging that indoor air has a special role as a health determinant and that the management of indoor air quality requires approaches different from those used for outdoor air, the working group preparing the global update of the WHO air quality guidelines *(3)* recommended that WHO should also prepare guidelines for indoor air quality. This is in line with the recommendations of an earlier WHO working group formulating a set of statements on "The right to healthy indoor air" and in particular with Principle 6, which states that "Under the principle of accountability, all relevant organizations should establish explicit criteria for evaluating and assessing building air quality and its impact on the health of the population and on the environment." *(4)*.

The WHO working group that subsequently met in Bonn in October 2006 acknowledged the applicability of the existing WHO guidelines for air quality *(2,3)*

to indoor air and identified a number of chemical substances for which specific indoor air guidelines should be recommended *(5)*. The working group also recommended developing guidelines for two additional categories of risk factor of particular importance for health in indoor environments: biological agents and indoor combustion. Following these recommendations, the WHO guidelines on dampness and mould were published in 2009 *(6)*.

The working group defined the following criteria for selecting compounds for which the development of WHO guidelines for indoor air could be recommended:

- existence of indoor sources
- availability of toxicological and epidemiological data
- indoor levels exceeding the levels of health concern (no observed adverse effect level (NOAEL) and/or lowest observed adverse effect level (LOAEL)).

Based on these criteria, pollutants considered were divided into two categories (Table 1). Group 1 included pollutants for which WHO guidelines for indoor air were needed and WHO was requested to plan their development. Group 2 included pollutants of potential interest, but the group concluded that further investigation would be needed before it was clear whether there was sufficient evidence to warrant their inclusion in the guidelines at present.

Table 1. Pollutants considered for inclusion in the WHO indoor air quality guidelines by the WHO working group in October 2006

Group 1. Development of guidelines recommended	Group 2. Current evidence uncertain or not sufficient for guidelines
Benzene	Acetaldehyde
Carbon monoxide	Asbestos
Formaldehyde	Biocides, pesticides
Naphthalene	Flame retardants
Nitrogen dioxide	Glycol ethers
Particulate matter ($PM_{2.5}$ and PM_{10})	Hexane
Polycyclic aromatic hydrocarbons, especially benzo-[*a*]-pyrene	Nitric oxide
Radon	Ozone
Trichloroethylene	Phthalates
Tetrachloroethylene	Styrene
	Toluene
	Xylenes

Source: WHO Regional Office for Europe *(5)*.

The group concluded that the WHO guidelines for environmental tobacco smoke (ETS) published in the second edition of *Air quality guidelines for Europe (2)*, stating that there is no evidence for a safe exposure level, are clear and still valid. Therefore, ETS is not included in the current work. Furthermore, the guidelines for other pollutants should be developed based on the assumption that ETS is eliminated from indoor spaces.

The steering group[1] assisting WHO in designing the indoor air quality guidelines concluded that there is no convincing evidence of a difference in the hazardous nature of particulate matter from indoor sources as compared with those from outdoors and that the indoor levels of PM_{10} and $PM_{2.5}$, in the presence of indoor sources of PM, are usually higher than the outdoor PM levels. Therefore, the air quality guidelines for particulate matter recommended by the 2005 global update *(3)* are also applicable to indoor spaces and a new review of the evidence is not necessary at present. Consequently, the work on developing indoor air quality guidelines for selected pollutants focused on nine out of the ten compounds listed in Group 1 of Table 1, i.e. all except particulate matter. As decided at the working group meeting in 2006, the guidelines are intended to address various levels of economic development, cover all relevant population groups, and allow feasible approaches to reducing health risks from exposure to the selected pollutants in various regions of the world.

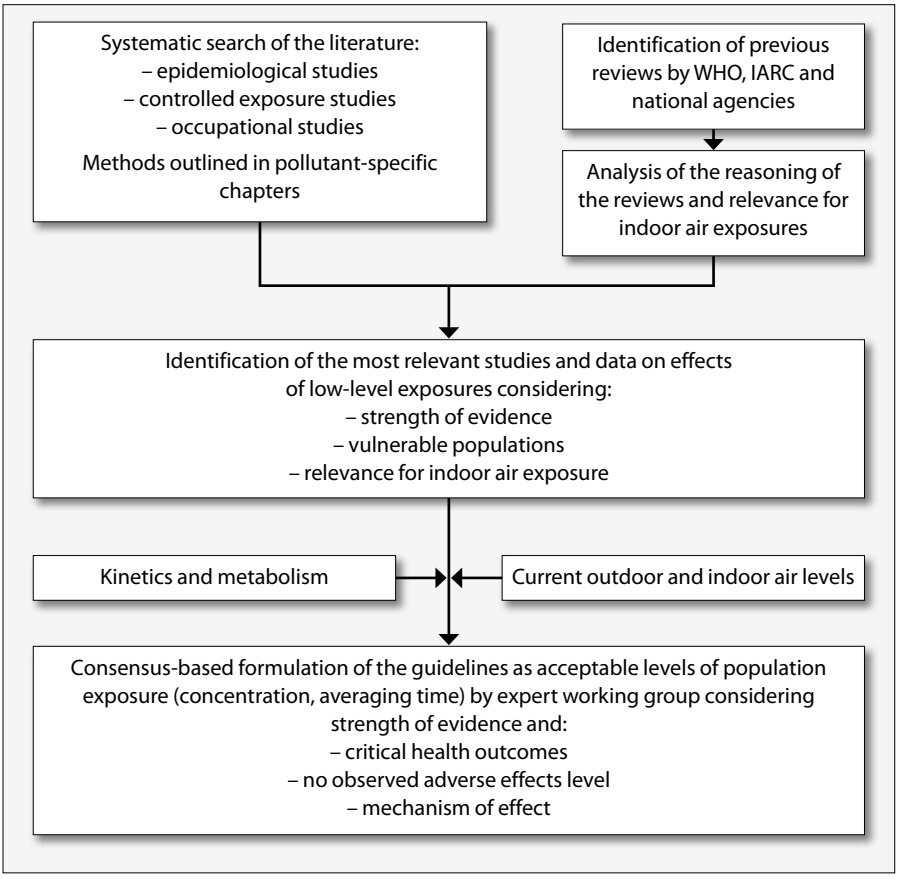
Setting indoor air quality guidelines

The general approach and terminology used in setting air quality guidelines has been presented in a previous WHO publication *(2)*. It is based on a careful review and interpretation of globally accumulated scientific evidence linking exposure to a selected pollutant in the air with the health outcomes of that exposure, using the approaches proposed by the WHO guidelines on assessing human health risks of chemicals *(7)* and on the evaluation of epidemiological evidence for environmental health risk assessment *(8)*. For each of the selected substances, a search of bibliographic databases was conducted to identify relevant studies, according to the search protocols described in each of the pollutant-specific chapters. Major reviews conducted by WHO, the International Agency for Research on Cancer (IARC) or national agencies were also considered an important source of information. The process followed in setting the guidelines is schematically presented in Fig. 1.

In reviewing the available information, a systematic review of the peer-reviewed publications was undertaken. This included specifically studies of the effects of indoor exposure to the compounds considered and also evidence gathered from studies of outdoor exposure. The evidence comes from epidemiological, toxicological and clinical research, examining associations between exposures to the pollutants and health as well as studying physiological mechanisms of the effects. The latter includes experiments based on controlled human exposure or using animals. Much of the available health evidence is indirect, based on exposures to mixtures of pollutants or to single pollutants in concentrations higher than usually encountered indoors. The advantages and disadvantages of

[1] Steering group members: Ross Anderson, Aaron Cohen, Severine Kirchner, Erik Lebret, Lars Mølhave, Aino Nevalainen, Bernd Seifert and Kirk Smith.

Fig. 1. The process followed in guidelines formulation



various types of study used to assess health effects of air pollution are summarized in introductory chapters of the 2005 global update *(3)*.

The review of the evidence focuses on the papers considered to be most relevant for development of the guidelines, and in particular on the studies providing quantitative links between health outcomes and the exposures (as determined by the concentrations of pollutants and the duration of exposure) encountered in indoor environments. The strength of evidence for a link between exposure and health outcome was classified according to the criteria used in the *WHO guidelines for indoor air quality: dampness and mould (6)*, based on the approach developed by the Institute of Medicine *(9)* and presented in Box 1. The evidence was classified according to the professional judgement of the experts of the clarity of the reported findings with consideration of the strength, quality, diversity and number of studies. Understanding of biological mechanisms responsible for associations observed in epidemiological studies, and described in the "kinetics and metabolism" sections of each pollutant-specific chapter, strengthened the conclusions reached.

BOX 1 Classifying the strength of evidence

The categories in this box refer to the association between exposure to an agent and a health outcome and not to the likelihood that any individual's health problem is associated with or caused by the exposure. These categories are used for classifying the evidence in this review, in the *WHO guidelines for indoor air quality: dampness and mould (6)* and in that of the Institute of Medicine *(9)*.

Sufficient evidence of a causal relationship
The evidence is sufficient to conclude that a causal relationship exists between the agent and the outcome. That is, the evidence fulfils the criteria for "sufficient evidence of an association" and, in addition, satisfies the following evaluation criteria: strength of association, biological gradient, consistency of association, biological plausibility and coherence and temporally correct association.

The finding of sufficient evidence of a causal relationship between an exposure and a health outcome does not mean that the exposure inevitably leads to that outcome. Rather, it means that the exposure *can* cause the outcome, at least in some people under some circumstances.

Sufficient evidence of an association
The evidence is sufficient to conclude that there is an association. That is, an association between the agent and the outcome has been observed in studies in which chance, bias and confounding could be ruled out with reasonable confidence. For example, if several small studies that are free from bias and confounding show an association that is consistent in magnitude and direction, there may be sufficient evidence of an association.

Limited or suggestive evidence of an association
The evidence is suggestive of an association between the agent and the outcome but is limited because chance, bias and confounding could not be ruled out with confidence. For example, at least one high-quality study shows a positive association, but the results of other studies are inconsistent.

Inadequate or insufficient evidence to determine whether an association exists
The available studies are of insufficient quality, consistency or statistical power to permit a conclusion regarding the presence or absence of an association. Alternatively, no studies of the association exist.

Limited or suggestive evidence of no association
Several adequate studies are consistent in not showing an association between the agent and the outcome. A conclusion of "no association" is inevitably limited to the conditions, magnitude of exposure and length of observation covered by the studies available.

In estimating the health risks of exposure, it was not possible to apply the techniques of formal meta-analysis to the evidence base; marked differences in study design and, in some cases, the very limited number of studies available made this impossible.

The evaluation of health risks, which follows the presentation of the most important studies, sets out the conclusions of the experts based on the accumulated evidence. It includes risk characterization (i.e. a summary, integration and evaluation of the major scientific evidence) and considers the relevance to health of

indoor exposures encountered in various non-occupational settings as well as the conclusions of other reviews.

Ideally, guideline values should represent concentrations of chemical compounds in air that would not pose any hazard to the human population. Realistic assessment of hazards to human health, however, necessitates a distinction between absolute safety and acceptable risk. To produce a guideline with a high probability of offering absolute safety, one would need a detailed knowledge of dose–response relationships in individuals in relation to all sources of exposure, the types of toxicological effect elicited by specific pollutants or their mixtures, the existence or non-existence of "thresholds" for specified toxicological effects, the significance of interactions, and the variation in sensitivity and exposure levels within the human population. Such comprehensive and conclusive data on indoor contaminants are generally unavailable. Very often, the relevant data are scarce and the quantitative relationships uncertain. The professional judgement of the scientists evaluating the evidence and consensus therefore play an important role in establishing guidance that can be used to indicate acceptable levels of population exposure. Value judgements are needed and the use of subjective terms such as "adverse effects" is unavoidable.

Distinction between adverse and non-adverse effects is difficult. For example, changes in a physiological variable such as an index of lung function that might be regarded as minor and reversible could imply a significant short- or perhaps long-term effect on health. In developing these guidelines, concerns were often expressed about the possible long-term effects of repeated insults that individually produce only small changes in physiological end-points. It was also noted that physiological changes that had previously been seen as indicative of only minor effects (such as a small increase in carboxyhaemoglobin concentration) might not explain all the effects of exposure to a pollutant.

Although it might be accepted that a certain risk can be tolerated, the risks to individuals within a population may not be equally distributed: there may be subpopulations that are at considerably increased risk. Therefore, groups at special risk in the general population must be taken specifically into account in the risk management process. Even if knowledge about groups with specific sensitivity is available, unknown factors may exist that change the risk in an unpredictable manner. During the preparation of these guidelines, attention was paid to defining specific sensitive subgroups in the population.

Preparation of the guidelines

As recommended by the working group that met in 2006 to plan the development of the guidelines, a steering group was established to advise on the scientific issues concerning their development. This group recommended potential authors, who would be invited to review the evidence and develop the first draft of the background material during the summer and autumn of 2008. The steer-

ing group also recommended other experts to act as reviewers of the background material. All invited experts, including the members of the steering group, are internationally recognized scientists conducting research in academic or public health institutions and active in the assessment of health risks related to exposure to chemicals. Their expertise includes exposure assessment, toxicology, epidemiology and risk assessment. All experts were requested to disclose any circumstances that could give rise to a potential conflict of interests, i.e. any interests that might affect or might reasonably be perceived to affect the experts' objectivity and independence. A standard "Declaration of interests for WHO experts" form was used, and any positive responses to a set of questions in the Declaration were evaluated by the WHO Legal Office and the representatives of the WHO Guidelines Review Committee. Only experts with no declared conflicts of interests, or for whom the declared activities were not considered to create such conflicts, participated in the formulation of the guidelines.

The background material on each of the nine pollutants reviewed contained sections on:

- general description of the compound;
- indoor sources and pathways of exposure;
- current indoor levels and relationship with outdoor levels;
- kinetics and metabolism (including experimental evidence on pathogenic mechanisms from animal and in vitro studies); and
- health effects.

The authors submitted the drafts to WHO in November/December 2008. The complete drafts on each of the compounds were distributed to the reviewers with a request that they evaluate the completeness of the scientific evidence used to prepare the manuscript, the scientific reliability of the evidence review and the clarity of the conclusions of the review. The comments received from the reviewers and collated by the WHO secretariat, were used by the authors to prepare the second drafts, including, in addition to the sections listed above, a first draft of the "Health risk evaluation" section. These second drafts were made available to the WHO working group in advance of its meeting in Bonn on 2–6 November 2009.

The working group meeting was convened to agree on the risk evaluation for each of the pollutants and to formulate WHO guidelines for protecting public health from these risks. Existing national and international guidelines, experience in indoor air quality regulation and the results of completed international reviews supported the discussion and its conclusions. The meeting brought together 47 experts from 15 countries, who had reviewed the evidence and prepared the background papers, as well as members of the steering group. It also involved three observers from national agencies potentially interested in using WHO indoor air quality guidelines in shaping policies and actions addressing

health risks of indoor air pollutants, as well as five scientists from WHO headquarters, the WHO Regional Office for Europe and IARC. Robert Maynard and Bernd Seifert chaired the meeting.

Several consecutive drafts of the guidelines section for each pollutant were prepared by small groups of experts and discussed in plenary. The final text was reviewed and approved by consensus at the plenary session. Besides agreeing on the health risk evaluations of the pollutants and formulating the guidelines sections, the experts provided comments on the final text of the background material. These comments were used by the authors to finalize the background sections summarizing the evidence supporting the guidelines in the two months following the meeting. The complete unedited draft was made available to all the working group members for final comments. Final changes to the background sections (but not in the guidelines), as well as to the boxes summarizing the main decisions leading to setting the guidelines, were made following language editing. The edited text was then reviewed by the WHO Guidelines Review Committee. Fig. 2 illustrates the major steps in the process leading to the publication of the guidelines.

Combined exposures

This volume contains an evaluation of the health effects of specific chemicals. However, exposure to combinations of air pollutants is inevitable. Data dealing with the effects of co-exposure to air pollutants are very limited and, in most cases, it is not possible to recommend guidelines for such combinations. Notable exceptions are guidelines on particulate matter, assessed on the basis of mass concentration of particles of a broad range of physical and chemical properties. Of course, measures taken to control air pollution frequently lead to the reduction in concentrations of more than one pollutant. This is often achieved by controlling sources of pollutants rather than by focusing on individual pollutants. This is especially important in the indoor environment. In developing countries, the use of solid fuel, often including biomass, in poorly ventilated buildings leads to exposure to a mixture of air pollutants. Combinations of pollutants can lead to additive or synergistic effects: the combinations of exposure to tobacco smoke and radon and asbestos fibres provide examples of synergistic effects. These are well-known effects. Less well-known is, for example, the possibility that cataract formation may be linked to exposure to the mixture of pollutants generated by burning biomass indoors. Whether this effect is due to a single pollutant or to co-exposure to a group of pollutants is unknown.

A good example of difficulty in attributing health effects to one of the components of indoor air pollution mixture is provided by particulate matter. The measures to assess or control particle mass concentration are rarely effective in respect to very small particles, often referred to as ultrafine (< 0.1 μm), and most commonly measured as number concentration. Operation of combus-

Fig. 2. Major stages in preparation of the WHO guidelines on indoor air quality: selected pollutants

tion sources always results in the emission of ultrafine particles as well as many other pollutants, and particularly as discussed in this document, benzene, carbon monoxide, nitrogen dioxide and polycyclic aromatic hydrocarbons. Possibly synergistic effects of exposure to these pollutants and ultrafine particles are not known at this point. It is also not known whether some of the pollutants act as surrogates for ultrafine particles (or vice versa).

Some of these problems will be addressed by the guidelines on indoor combustion, to be developed following the recommendations of the WHO work-

ing group from 2006 *(5)*. Nevertheless, it is important to emphasize the need to consider the health risks of all pollutants for which guidelines are available in activities to improve indoor air quality. This, to some extent, is addressing the health hazard of combined exposure. Furthermore, situations where following the guideline for one pollutant adversely affects other aspects of indoor air quality should be avoided.

When strategies to protect public health are under consideration, the air quality guidelines on selected substances need to be placed in the perspective of total chemical exposure. The interaction of humans and the biosphere is complex. Individuals can be exposed briefly or throughout their lifetimes to chemicals in air, water and food; exposures may be environmental or occupational. In addition, individuals vary widely in their response to exposure to chemicals; each person has a pre-existing status (defined by, for example, age, sex, pregnancy, pulmonary disease, cardiovascular disease, genetic make-up) and a lifestyle, in which such factors as exercise and nutrition play key roles. All these different elements may influence a person's susceptibility to chemicals.

Use of the indoor air quality guidelines in protecting public health

The primary aim of these guidelines is to provide a uniform basis for the protection of public health from adverse effects of indoor exposure to air pollution, and to eliminate or reduce to a minimum exposure to those pollutants that are known or are likely to be hazardous. The guidelines are targeted at the public health professionals involved in preventing health risks of environmental exposures, as well as the specialists and authorities involved in the design and use of buildings, indoor materials and products. The guidelines are based on the scientific knowledge available at the time of their development. They have the character of recommendations, and it is not intended or advocated that they be adopted as standards. Nevertheless, countries may wish to transform the recommended guidelines into legally enforceable standards.

In the process of moving from a "guideline" or a "guideline value" to a "standard", a number of factors beyond the exposure–response relationship need to be taken into account. These factors include current concentrations of pollutants and exposure levels of a population, the specific mixture of air pollutants and the specific social, economic and cultural conditions encountered. In addition, the standard-setting procedure may be influenced by the likelihood of implementing the standard. Broader discussion of these considerations has been presented in an earlier edition of the WHO air quality guidelines *(2)*.

Establishing legally binding concentration-based standards of indoor air quality requires, inter alia, determination of the methods for enforcement of the regulation, including compliance testing. This poses difficulties for the use of standards as a means of reducing the effects on health of indoor exposure to air pollutants. Routine monitoring in people's homes is unlikely to be widespread,

and the application of measures to enforce standards is often not feasible or, at least, difficult.

The concentrations of pollutants in both indoor and outdoor air can be reduced by controlling the primary factor that determines their presence in the air: their sources. In the outdoor environment, this is all that can be done because the secondary factors that control concentrations – dispersion and dilution – are not generally under control as they depend largely on meteorological conditions. In the indoor environment, dispersion (to and from the outdoor environment) can be influenced by controlling the ventilation of the indoor space. This provides an additional means of changing indoor concentrations of pollutants. It also creates a difficulty: a source that might be entirely acceptable as regards output of pollutants in a well-ventilated space might be unacceptable in a poorly ventilated space. Of course, significant indoor sources should not be allowed to release pollutants into the indoor space: conducting pollutants to the outside space by flues and chimneys is clearly desirable. It should be noted, however, that indoor sources can make a substantial contribution to outdoor concentrations, especially in places where there are large, widespread sources of indoor pollution. This should be avoided by control of emission from indoor sources.

Thus, acceptable indoor air quality can be achieved through source control and pollutant dispersion, and in particular through:

- application of low-emission materials and products;
- proper selection of the devices and fuels used for combustion indoors;
- the venting of products to the outdoor air; and
- ventilation control.

In many countries, these means of control are encapsulated in product standards and building standards or regulations. In practice, both sets of standards are derived from calculations or experiments and are implemented without routine monitoring of pollutant levels indoors. Surveys of indoor concentrations of pollutants act as a means of checking that the standards are appropriate or, more often, that they are being appropriately applied. Here there is another difference between the approaches taken indoors and outdoors: monitoring outdoor concentrations of air pollutants is standard practice in many countries but routine monitoring of indoor concentrations hardly exists.

The development of product and building standards requires targets for acceptable indoor concentrations of air pollutants: here guidelines can play an important role. This is not very different from the approach adopted outdoors. Even in periods of high outdoor concentrations of air pollution, reduction of emissions is seldom more than an ad hoc solution, although reducing vehicle usage or industrial emissions at such times has been tried in a number of cities. Much more important than this are calculations based on inventories of sources and atmospheric dispersion modelling that form the basis of "product standards" as

applied, for example, to motor vehicle engines and to the fuels they burn, i.e. to the permanent characteristics of the sources. Such calculations are easier when applied to outdoor air; the wide range of types of dwelling and their levels of ventilation makes calculations more difficult for the indoor environment. Nevertheless, adoption of the guidelines presented in this volume as benchmarks for such models and actions is a useful option for reducing the adverse effects of indoor air pollution on health.

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1. Benzene

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General description

Benzene (CAS Registry Number 71-43-2; C_6H_6; molecular weight 78.1 g/mol) is an aromatic compound with a single six-member unsaturated carbon ring. It is a clear, colourless, volatile, highly flammable liquid with a characteristic odour and a density of 874 kg/m^3 at 25 °C *(1)*.

At 1 atmosphere of pressure, benzene has a melting point of 5.5 °C, a relatively low boiling point of 80.1 °C and a high vapour pressure (12.7 kPa at 25 °C), causing it to evaporate rapidly at room temperature. It is slightly soluble in water (1.78 g/l at 25 °C) and is miscible with most organic solvents *(2)*. Benzene is soluble in lipids, has a log K octanol–water partition coefficient of 2.14 *(1)* and a log K soil organic carbon–water partition coefficient of 1.85 at 25 °C. Its Henry's Law constant is 550 Pa.m^3/mol at 25 °C, implying that it will have a tendency to volatilize into the atmosphere from surface water *(3)*.

Benzene in air exists predominantly in the vapour phase, with residence times varying between one day and two weeks, depending on the environment, the climate and the concentration of other pollutants. Reaction with hydroxyl radicals is the most important means of degradation, with a rate constant of 1.2×10^{-12} cm^3.molecule^{-1}.s^{-1} at 298 K *(4)*.

Other oxidants such as ozone and nitrate radicals can also contribute to a lesser extent to the degradation of benzene indoors, with rate constants of 2.7×10^{-17} cm^3.molecule^{-1}.s^{-1} at 298 K for nitrate radicals *(5)* and 1.7×10^{-22} cm^3.molecule^{-1}.s^{-1} at 298 K for ozone *(1–3,6,7)*.

Conversion factors

At 760 mmHg and 20 °C, 1 ppm = 3.248 mg/m^3 and 1 mg/m^3 = 0.308 ppm; at 25 °C, 1 ppm = 3.194 mg/m^3 and 1 mg/m^3 = 0.313 ppm.

Indoor sources

Benzene in indoor air can originate from outdoor air and also from sources indoors such as building materials and furniture, attached garages, heating and cooking systems, stored solvents and various human activities. Indoor concentrations are also affected by climatic conditions and the air exchange rate due to forced or natural ventilation.

Indoor concentrations are affected by outdoor levels owing to the exchange of indoor and outdoor air. Outdoor benzene concentrations are mainly due to traffic sources and are affected by season and meteorology. Other outdoor sources of benzene are petrol stations and certain industries such as those concerned with coal, oil, natural gas, chemicals and steel *(8)*.

Materials used in construction, remodelling and decorating are major contributors to indoor benzene concentrations *(9)*. Certain furnishing materials and polymeric materials such as vinyl, PVC and rubber floorings, as well as nylon carpets and SBR-latex-backed carpets, may contain trace levels of benzene. Benzene is also present in particleboard furniture, plywood, fibreglass, flooring adhesives, paints, wood panelling, caulking and paint remover *(3,10,11)*. Therefore, new buildings or recently redecorated indoor environments have been associated with high concentrations of benzene from materials and furniture. The rate of emission of benzene from materials and furniture will decay and eventually these sources will reach a quasi-steady emission rate in new buildings within weeks or months or up to a year *(12)*.

Attached garages are a potential source of gasoline vapour owing to evaporation and exhaust emissions. In addition to cars, petrol, oil, paint, lacquer and hobby supplies often stored in garages can lead to increased levels of benzene indoors *(13)*. Some 40–60% of benzene indoors may be attributable to the presence of an attached garage *(13–16)*, with indoor benzene concentrations rising to 8 $\mu g/m^3$ when garages are connected to the main living environment *(14)*.

The use of fuels such as coal, wood, gas, kerosene or liquid petroleum gas (LPG) for space heating and cooking leads to higher concentrations of benzene indoors *(17–20)*.

The problem of indoor pollution from the use of domestic cooking stoves attains greater importance in developing countries owing to poor ventilation and the extensive use of low-efficiency stoves and biofuels. Benzene concentrations of 44–167 $\mu g/m^3$ have been found to be associated with the use of kerosene stoves *(21)*.

In the past, benzene was widely used as a solvent, mainly in industrial paints, paint removers, adhesives, degreasing agents, denatured alcohol, rubber cements and arts and crafts supplies. The imposition of lower occupational exposure limits led to a reduction in these uses *(3)* but benzene content may still be an issue in some parts of the world, such as some African countries.

Indoor benzene is also associated with human activities such as cleaning *(18)*, painting *(18,22,23)*, the use of consumer products *(24)* and mosquito repellents *(25)*, photocopying *(26)* and printing *(27)*, the storage and use of solvents, and smoking tobacco.

Environmental tobacco smoke (ETS) is considered one of the main indoor sources of benzene. Benzene emissions from cigarette smoking range from 430 to 590 μg per cigarette *(28)*. An increase in benzene concentration of at least 30–

70% is expected *(3,18,20,29,30)* when ETS is present indoors, with increases in some cases of 300% *(31)* to levels of 16 μg/m^3 *(18)*.

To sum up, outdoor benzene provides the baseline for benzene concentrations indoors, upon which will be superimposed benzene given off from building materials and indoor artefacts. The presence of attached garages and combustion sources (especially smoking) and other human activities will be the main determinant of the concentration of benzene indoors.

Pathways of exposure

Inhalation accounts for more than 95–99% of the benzene exposure of the general population, whereas intake from food and water consumption is minimal *(3,32)*. In the United States, daily benzene intake from ambient and indoor air has been calculated to range between 180 and 1300 μg/day, and that in food and water up to about 1.4 μg/day *(2)*. The average daily intake for an adult in Canada was estimated to be 14 μg/day from ambient air, 140 μg/day from indoor air, 1.4 μg/day from food and drinking-water and 49 μg/day from car-related activities, giving a total of about 200 μg/day *(33)*. Wallace *(30)* estimated the corresponding average intake in the United States to be 320 μg/day.

Cigarette smoking has been found to contribute significantly to the amount of benzene inhaled *(34)*. Exposure to ETS is widespread in most countries *(35)*. A survey conducted in the United States in 2006 found that more than 40% of non-smoking adults and almost 60% of children aged 3–11 years were exposed to ETS *(36)*. Another survey, conducted among young people in 132 countries, found that 44% had been exposed to ETS at home and 56% in public places, while another survey found that the exposure of young people at home ranged between 30–87% and 53–98% in public places *(37)*. Active smoking may add as much as 400–1800 μg/day *(2,34)*, while inhalation due to passive smoking will represent an additional 14–50 μg/day to the average daily intake *(2,38)*. Driving a car during the rush hour may give a significant additional intake of 20 μg/day *(34,39)*. Fromme *(40)* calculated the relative intake from food and uptakes from ambient air, indoor air and air inside cars to be 8%, 9%, 53% and 30%, respectively. In a study carried out in Germany in the 1990s, it was found that indoor exposure to ETS and car-related activities (refuelling and time in transit) could account for 20% and 12%, respectively, of personal exposure to benzene *(2)*.

A study carried out in the United Kingdom estimated a daily dose of benzene of 70–75 μg/day for rural non-smokers and 89–95 μg/day for urban non-smokers. The daily dose rose to 116–122 μg/day for urban passive smokers and to over 500 μg/day for urban smokers. Children's daily exposures were estimated to be 15–20 μg/day and 30–40 μg/day for infants and children, respectively, while exposure to ETS led to a daily exposure of 26 μg/day and 59 μg/day for a urban infants and children, respectively *(34)*. Most of the children's exposures were produced in the home *(41)*.

A European study estimated a daily inhaled benzene dose of 102 μg/day, where 36%, 32%, 2% and 30% of the exposure was attributed to indoor home, indoor work, outdoor and in transit, respectively *(42)*. In some Asian cities, where high levels of benzene were reported in homes and offices *(25,43)*, the daily inhalation dose of benzene from indoor sources can be as high as 480–580 μg/day.

Indoor concentrations

Mean indoor concentrations are typically higher than the respective ambient levels and have been consistently shown to be higher in the colder than the warmer seasons *(16,44,45)*. Indoor levels measured in the United States are in the range 2.6–5.8 μg/m^3 *(13,14,46,47)*, which are levels similar to those measured in established buildings in Australia *(22)* and Europe *(48)*.

In European cities, a trend has been observed of increasing indoor concentrations from north to south. Low indoor concentrations (2 μg/m^3) were measured in Finnish homes *(49)*, while they ranged from 2 to12 μg/m^3 in central European cities *(17,44,50–54)* and from 10 to 13 μg/m^3 in southern cities such as Milan and Athens *(48)*. Indoor levels measured in Turkey were in the range 7–14 μg/m^3 *(55)*.

Studies carried out in Asian cities have found much higher indoor benzene concentrations than those reported from cities in the developed world. Houses in India that used kerosene stoves were reported as having average indoor levels of 103 μg/m^3 *(21)*. Higher concentrations have been reported from some Chinese cities, with levels as high as 57.4 μg/m^3 in Guanzhou *(56)*. On the other hand, indoor levels of benzene in Japan are similar to those found in Australia, Europe and the United States, with arithmetic mean values ranging from 0.7 to 7.2 μg/m^3 *(45,57–59)*.

Indoor concentrations in buildings in Singapore were 18.4–35.4 μg/m^3 *(43)*, and similar levels of 23–35 μg/m^3 were found in the Republic of Korea *(25)*. However, a previous study in the Republic of Korea at the end of the1990s found lower concentrations (8.2 μg/m^3 in homes and 12.6 μg/m^3 in offices) than those reported in 2003 by Son et al. *(60)*. Another study performed in India reported indoor concentrations of 10.7 μg/m^3 *(23)*. The lowest concentrations were reported from the Hong Kong Special Administrative Region of China (Hong Kong SAR), with values of 0.5–4.4 μg/m^3 in different indoor environments such as houses, offices and shopping centres *(61,62)*.

Cigarette smoke is an important source of benzene in indoor air, and benzene concentrations measured indoors increase when ETS is present *(2)*. Indoor benzene levels measured in the United States showed arithmetic values of 5.54–10.5 μg/m^3 in homes exposed to ETS compared to 3.86–7.0 μg/m^3 in ETS-free homes *(20,63)*. A similar situation was reported in Italy, with levels of 32.2 and 18.9 μg/m^3 in ETS and ETS-free homes, respectively *(64)* and in Germany, with levels of 11.0 and 6.5 μg/m^3, respectively *(40)*.

Indoor concentrations measured in offices are generally higher than those measured in residential buildings, owing to the presence of sources such as photocopiers and printers. The mean office level in eight European countries was 14.6 μg/m^3, while 87.1 μg/m^3 was measured inside an office in Singapore *(43)*. A recent study in United Kingdom offices reported lower benzene levels in the range of 0.4–4.0 μg/m^3 (1.3 μg/m^3 arithmetic mean) *(53)*.

Benzene levels measured in restaurants ranged from 1.1 to 22.7 μg/m^3, while higher levels of 5.1–78.8 μg/m^3 were reported in pubs *(18,53,60,61,65,66)*, with discotheques/clubs being the locations with the highest mean concentrations (193 μg/m^3) in a study carried out in Germany *(66)*. Benzene concentrations measured in several public indoor spaces such as shopping centres, libraries and cinemas ranged from 0.7 to 15.5 μg/m^3 *(18,53,62)*.

Benzene concentrations measured in vehicles are generally higher than those outdoors. Levels of benzene measured in vehicles in Europe ranged from 13 to 42 μg/m^3 (65,67), while lower levels of 1.3–3.8 μg/m^3 were measured in a recent United Kingdom study *(53)*. Benzene levels measured in Mexico and the United States ranged from 1.7 to 42 μg/m^3 *(68,69)* and a similar range (0.5–47 μg/m^3) was found in several Asian cities *(61,70)*. The highest in-vehicle benzene levels were measured in Italy in the early 2000s, with geometric means ranging from 17 to 101 μg/m^3 *(64)*.

Relatively high benzene concentrations indoors have been attributed to sources such as incense burning, with benzene concentrations peaking at up to 117 μg/m^3 *(48)*; new buildings (e.g. up to 30 μg/m^3) *(22)*; attached garages (e.g. 16–19 μg/m^3); tobacco smoke (e.g. 16–193 μg/m^3) *(18,23,66)*; cleaning (e.g. 13 μg/m^3) *(18)*; painting (e.g. 9–13 000 μg/m^3) *(18,23)* and using a kerosene stove (e.g. 166 μg/m^3) *(21)*.

Indoor–outdoor relationship

Indoor concentrations of benzene are normally higher than those in outdoor air *(9)* as a consequence of the entry and accumulation of benzene from outdoor sources and the presence of dominant benzene sources indoors. Viewed across published studies, indoor concentrations of benzene ranged from 0.6 to 3.4 (arithmetic mean 1.8) times the outdoor concentrations and are greatly influenced by those outdoors. This occurs in part because there are numerous indoor sources of benzene and because the relatively low rates of ventilation typically used in residences and offices prevent the rapid dispersal of airborne contaminants *(9)*.

Indoor–outdoor ratios close to unity (i.e. 0.96–1.10) have been reported in some Asian countries where outdoor air concentrations were particularly high (25–35 μg/m^3) *(25,55,60,71)*. High indoor–outdoor ratios have been traditionally associated with strong indoor sources such as attached garages (ratio > 3) *(13,14)*, combustion sources such as kerosene stoves (ratio 3.3) *(21)*, gas and charcoal cooking (ratio 2) *(60)* or ETS (ratio 1.6–2) *(23,48,60)*.

Kinetics and metabolism

The toxicity of benzene is dependent on its metabolism, as shown by its lower toxicity (*a*) in the presence of toluene, an inhibitor of benzene metabolism; (*b*) in animals that have had a partial hepatectomy; and (*c*) in mice that lack the enzyme CYP2E1 *(72)*. Many studies have been completed in animals and to some extent in humans to determine the metabolism of benzene and its toxicokinetics.

Toxicokinetics

Absorption

Following inhalation exposure, the fraction absorbed is concentration-dependent, with a higher fraction absorbed at lower concentrations. In rats exposed for six hours to 11 or 130 ppm benzene, approximately 95% of the inhaled benzene was absorbed, while only 52% was absorbed after exposure to 930 ppm benzene *(73)*.

Two studies in humans indicate that 50% of the quantity of inhaled benzene is absorbed *(74,75)*. Cigarette smoke is a source of benzene exposure; the benzene concentration in the blood of 14 smokers was significantly higher (median 493 ng/l) than that in 13 non-smokers (median 190 ng/l) *(76)*. Absorption of benzene is also rapid via the oral and dermal routes. Rats absorb and rapidly metabolize oral doses of benzene up to approximately 50 mg/kg. However, after an oral dose of 150 mg/kg, about 50% of the dose is exhaled as non-metabolized benzene *(73)*.

Distribution

After entry into the human organism, benzene is distributed throughout the body and, owing to its lipophilic nature, accumulates preferentially in fat-rich tissues, especially fat and bone marrow. In humans, benzene crosses the blood–brain barrier and the placenta and can be found in the brain and umbilical cord blood in quantities greater than or equal to those present in maternal blood *(77,78)*.

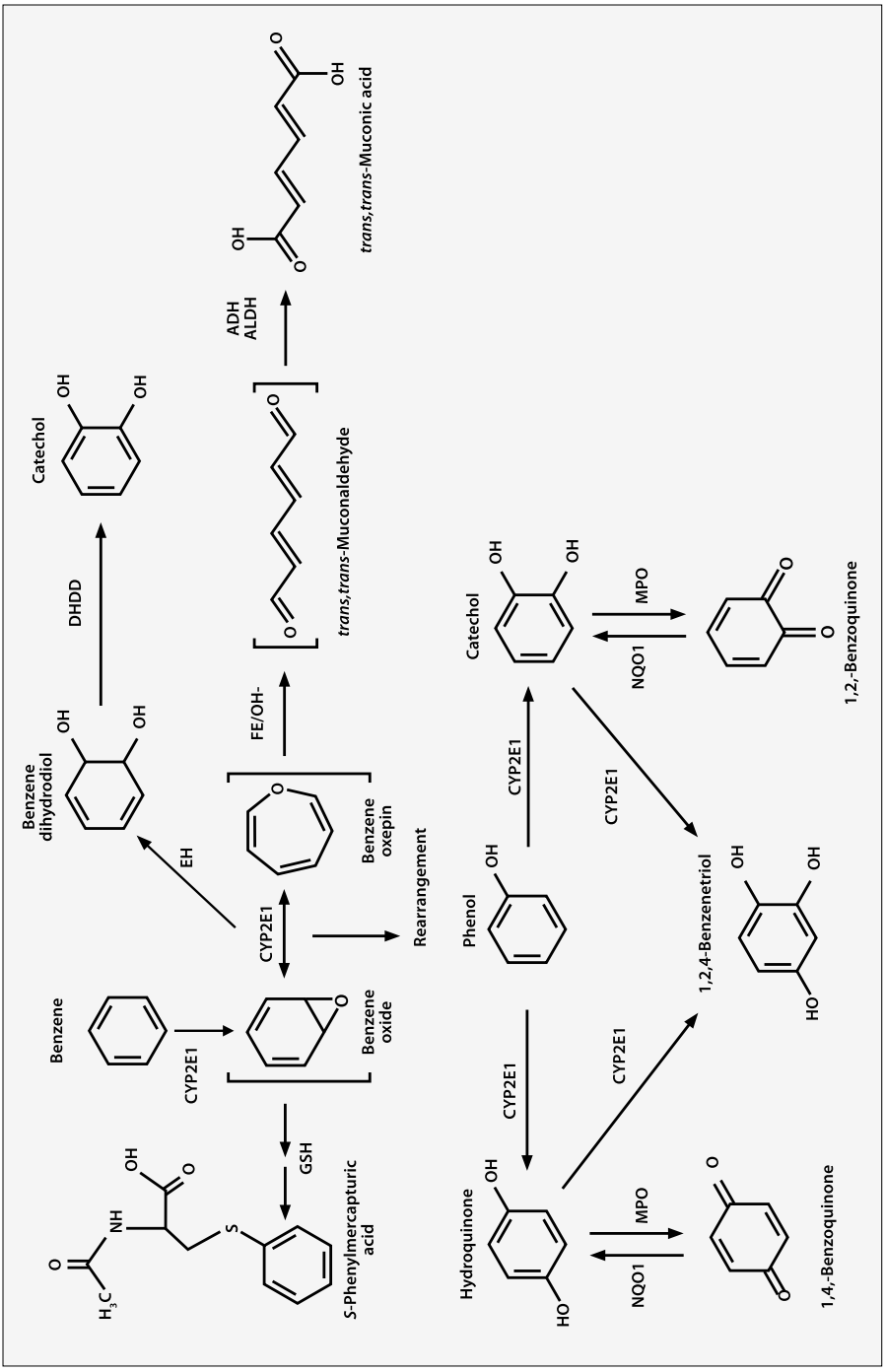
Elimination

Following all routes of exposure in rats and mice, absorbed benzene is rapidly metabolized (mostly within 48 hours), mainly by the liver, and approximately 90% of the metabolites are excreted in the urine *(72)*. Elimination of non-metabolized benzene is by exhalation.

Metabolism

Qualitatively, the metabolism and elimination of benzene appear to be similar in humans and laboratory animals *(79)*. Benzene is metabolized mainly in the liver but also in other tissues, such as the bone marrow. A diagram of benzene metabolism is presented in Fig. 1.1 *(80)*.

Fig. 1.1. Metabolism of benzene



Source: Agency for Toxic Substances and Disease Registry *(80)*.

Note: ADH: alcohol dehydrogenase; ALDH: aldehyde dehydrogenase; CYP 2E1: cytochrome P450 2E1; DHDD: dihydrodiol dehydrogenase; EH: epoxide hydrolase; GSH: glutathione; MPO: myeloperoxidase; NQO1: NAD(P)H:quinone oxidoreductase.

The first step consists in oxidation to benzene oxide and benzene oxepin (formation in equilibrium). This step is mainly catalysed by the enzyme CYP2E1 *(81)*. There are three major pathways by which benzene oxide is further metabolized. It can go through a series of ring-breakage reactions to form t,t-muconaldehyde, which is further oxidized to the acid; it can go through a series of reactions to form a conjugate with glutathione, which is eventually excreted in the urine as phenyl mercapturic acid; or it can rearrange non-enzymatically to form phenol *(82)*.

Phenol can be excreted in the urine directly or it can be further oxidized by CYP2E1 to catechol or hydroquinone. Catechol can be oxidized to trihydroxybenzene, and hydroquinone can be oxidized to the highly reactive bipolar benzoquinone. All of the phenolic compounds can form conjugates (glucuronides or sulfates) and be excreted in the urine *(72,83–86)*. The enzyme myeloperoxidase (MPO), which is present in bone marrow, can also oxidize phenolic compounds into quinones *(79,87–89)*.

The metabolites responsible for benzene toxicity are not yet fully understood. The key toxic metabolites for cytotoxicity and the induction of leukaemia are thought to be benzoquinone, benzene oxide and muconaldehyde *(1,90–95)*. The genotoxic activity of benzene metabolites is thought to be clastogenic (causing chromosomal damage) rather than acting through point mutations (see section on mechanism of action below). Benzoquinone and muconaldehyde are both reactive, bipolar compounds known to be clastogenic and the pathways leading to their formation are favoured at low concentrations in both mice and humans *(72,96,97)*.

Two enzymes are active in the detoxification of benzene metabolites *(98)*. One is NAD(P)H:quinone oxidoreductase (NQO1), which reduces the quinone metabolites to the less toxic diols *(87,99)*; the other is the microsomal epoxide hydrolase, which hydrolyzes the epoxide group on benzene oxide.

There are species differences in the metabolism of benzene. Rats convert most of the benzene to phenol, a marker of a detoxification pathway, while mice form greater amounts of hydroquinone, hydroquinone glucuronide and muconic acid, all markers of toxification pathways. Human metabolism resembles that of mice, the species more sensitive to benzene toxicity *(79,100–102)*.

Biomarkers of exposure

In the past, urinary phenol was commonly used as a biological exposure index in industrial settings to evaluate the exposure of workers to benzene. However, phenol is a good marker only of high-level benzene exposure and, with increased regulation of exposures, urinary phenol is no longer sensitive enough to be useful. More sensitive than phenol are urinary S-phenyl mercapturic acid and t,t-muconic acid, but the most sensitive exposure biomarker studied so far is the parent compound, benzene, in the urine *(103,104)*.

Polymorphisms

Polymorphisms in genes involved in benzene metabolism are thought to influence individual susceptibility to various levels of benzene exposure. Lin et al. *(105)* concluded that, among the GST genotypes investigated, only the GSTT1 genotype was related to the level and dose-related production of S-phenyl mercapturic acid.

NQO1 also exists in polymorphic form. The wild NQO1*1 allele encodes the normal enzyme NQO1, whereas the NQO1*2 allele encodes a mutated NQO2 enzyme presenting negligible activity. Approximately 5% of the Caucasian and Afro-American population, 15% of the American–Mexican population and 20% of the Asian population are homozygotes for the NQO1*2 allele *(106,107)*. Rothman et al. *(108)* demonstrated that workers in which the enzymatic activity of NQO1 was negligible presented a higher risk of benzene poisoning. The same is true for those expressing a rapid cytochrome CYP2E1 activity. Workers who simultaneously had a negligible NQO1 activity and a rapid CYP2E1 had a sevenfold higher risk of benzene poisoning than workers not presenting this dual polymorphism. Deletion of the glutathione S-transferase T1 (GSTT1) gene also showed a consistent quantitative 35–40% rise in DNA single strand break (DNA-SSB) levels.

Mechanism of action

In addressing the mechanism of action of benzene toxicity, one must consider two types of toxicity. At high exposure levels, benzene acts as a narcotic that depresses the central nervous system and causes cardiac sensitization *(109)*. The study of the mechanism for induction of leukaemia and other haematotoxic effects from low-level chronic exposures to benzene has been hampered by the lack of a good animal model for the induction of acute myeloid leukaemia, the major toxic end-point observed in humans. As mentioned above, benzene acts mainly as a clastogenic agent, rather than causing point mutations. The benzoquinones and t,t-muconaldehyde have dual reactive sites that make them capable of clastogenic activity towards DNA. The phenolic metabolites formed in the liver can be transported in the blood to the bone marrow, a major site for toxic effects, and be oxidized to the highly reactive quinones by myeloperoxidases in the marrow. The reactive quinones can cause clastogenic damage to the DNA, such as mitotic recombinations, chromosome translocations and aneuploidies *(110,111)*.

The observed effects of benzene may also be due to the metabolite, benzene oxide. Benzene oxide adducts have been found in the blood (haemoglobin) and bone marrow of mice exposed to benzene *(112)*. Benzene oxide and its adducts have been detected in the blood of workers exposed to benzene *(113–117)*. The studies by Liu et al. *(118)* and Nilsson et al. *(119)* suggested that the metabolites of benzene activate oxygenated radical species, which can lead to DNA changes and the formation of hydroxylated bases such as 8-hydroxy-2-deoxyguanosine.

The toxicity of benzene may also be due to combinations of metabolites *(83–86)*. All the non-conjugated metabolites of benzene, with the exception of phenol and 1,2,4-benzenetriol, are known to induce a reduction in erythropoiesis *(120)*. In mice, a mixture of phenol and hydroquinone induces an increase in loss of cellularity of the bone marrow and an increase in DNA modification *(85,121)*. Phenol–hydroquinone or phenol–catechol mixtures are more toxic for the haematopoietic system than the metabolites alone *(122)*. Catechol stimulates the activation of hydroquinone via peroxidase and triggers a genotoxic effect on lymphocytes, which is amplified in comparison with hydroquinone alone.

Health effects

Identification of studies

The acute non-carcinogenic effects of exposure to high concentrations of benzene and the carcinogenic effects of long-term exposure to lower concentrations are well-established research fields. Therefore, the sections on health effects and toxicokinetics are based on a consultation of summary reports published by various organizations up to December 2006: IARC (*123)*, the Agency for Toxic Substances and Disease Registry (ATSDR) *(80)*, the US Environmental Protection Agency (USEPA) (*124)*, the European Commission (*48)*, INERIS *(125)*, WHO (*2)* and the summary document produced by IARC in 2009 (*126)*.

The sections on mechanisms of action of benzene were supplemented by expert knowledge and by a search in the database PubMed with the following keywords: benzene and health effects, metabolism, kinetics, cancer, leukaemia, genetic polymorphism. This search revealed 37 published papers related to mechanisms of carcinogenicity of benzene up until 2008.

Non-carcinogenic effects

Acute non-carcinogenic effects

There are many reports of human deaths from inhaling high concentrations of benzene *(127,128)*. Death occurred suddenly or a few hours after exposure. The benzene concentrations to which the victims were exposed were often not known. However, it has been estimated that exposure to 20 000 ppm (64 980 mg/m^3) for 5–10 minutes is generally fatal and associated with cerebrovascular ischaemia *(129)*. Death is often attributed to asphyxia, respiratory arrest or central nervous system depression. When autopsies could be performed, cyanosis, haemolysis and ischaemia or haemorrhage of the organs were observed *(127,130,131)*.

In mild forms of poisoning, excitation is reported followed by speech problems, headaches, dizziness, insomnia, nausea, paraesthesia in the hands and feet and fatigue. These symptoms are generally observed for benzene concentrations ranging between 300 and 3000 ppm (975–9750 mg/m^3) *(128,129,132)*. More exactly, inhalation of 50–100 ppm (162–325 mg/m^3) for 30 minutes leads to fatigue

and headaches, while 250–500 ppm (812–1625 mg/m^3) causes dizziness, headaches, faintness and nausea.

INRS (the French National Research and Safety Institute) *(133)* gives the following thresholds for neurological symptoms triggered by acute exposure to benzene: no effect at 25 ppm (81 mg/m^3), headaches and asthenia from 50 to 100 ppm (162–325 mg/m^3), more accentuated symptoms at 500 ppm (1625 mg/m^3), tolerance for only 30–60 minutes at 3000 ppm (9720 mg/m^3) and death in 5–15 minutes at 20 000 ppm (64 980 mg/m^3).

Subchronic and chronic effects

Haematological effects. It is well known from numerous epidemiological studies conducted among workers that subchronic or chronic exposure to benzene leads to adverse haematological effects. Most of these blood effects (aplastic anaemia, pancytopenia, thrombocytopenia, granulopenia, lymphopenia and leukaemia) have been associated with inhalation exposure.

Bone marrow alteration is one of the first signs of chronic benzene toxicity. Aplastic anaemia is one of the most severe effects; the stem cells never reach maturity. Aplastic anaemia can progress to a myelodysplastic syndrome, and then to leukaemia *(134)*. Cytokine changes and chromosomal abnormalities are proposed explanations of the progression of aplastic anaemia to myeloproliferative syndrome and development of leukaemia (see the section on carcinogenic effects below).

Numerous studies conducted by Aksoy have described haematotoxicity. In a population of 217 male workers exposed for between 4 months and 17 years to a concentration of 15–30 ppm (48.8–97.5 mg/m^3), 51 developed leukopenia, thrombocytopenia, eosinophilia and pancytopenia *(135)*. In an additional cohort including 32 people working in the shoe industry, who used benzene for between 4 months and 15 years and were exposed to concentrations of 15–30 ppm (49–98 mg/m^3) outside working hours or 210–640 ppm (683–2080 mg/m^3) during their work, the workers developed pancytopenia with bone marrow changes *(136)*. In another study, conducted 2–17 years following the last exposure to benzene, 44 patients presented with pancytopenia following exposure to concentrations of 150–650 ppm (487.5–2112.5 mg/m^3) for between 4 months and 15 years *(137)*.

The study by Li et al. *(138)*, conducted over the period 1972–1987, examined 74 828 workers exposed to benzene in 672 factories and 35 805 workers not exposed to benzene in 109 factories, the factories studied being located in 12 Chinese cities. A slight increase in the relative risk of developing a lymphoproliferative disorder in both sexes was observed among workers from the chemicals, rubber and paint industries. Rothman et al. *(139,140)* compared 44 men and women exposed to 31 ppm (101 mg/m^3) as median 8-hour time-weighted average with 44 paired control subjects. The numbers of white blood cells, lym-

phocytes, platelets and red blood cells and the haematocrit were lower in exposed subjects. In a subgroup of 11 workers with a mean exposure value of 7.6 ppm (25 mg/m^3) with no exposure over 31 ppm (101 mg/m^3), only the absolute number of lymphocytes was significantly reduced. However, after having conducted a retrospective, longitudinal study on a cohort of 459 rubber workers, Kipen et al. *(141)* observed a negative correlation between benzene concentration and the number of white blood cells. These data were re-analysed by Cody et al. *(142)*, who reported a significant reduction in the number of white and red blood cells in a group of 161 workers compared with data before exposure for the period 1946–1949.

Results reported for exposures below 1 ppm (3.25 mg/m^3) showed a significant reduction in the number of red blood cells, leukocytes and neutrophils. For example, Qu et al. *(143,144)* observed such decreases in 130 workers chronically exposed to benzene at 0.08–54.5 ppm (0.26–177 mg/m^3) compared to a control group of 51 non-exposed workers. Even those in the lowest exposure group (0.82 mg/m^3 and lower) showed reductions in circulating red and white blood cells. Lan et al. *(145)* studied 250 Chinese workers exposed to benzene for a mean duration of 6.1 years (± 2.9 years) and 140 Chinese workers not exposed to benzene. Three groups of workers were studied on the basis of their exposure level: < 1 ppm, from 1 to < 10 ppm and ≥ 10 ppm (< 3.25 mg/m^3, from 3.25 to < 32.5 mg/m^3 and ≥ 32.5 mg/m^3). The control population worked in a factory where benzene concentrations were below the limit of detection (0.04 ppm or 0.13 mg/m^3). For a mean exposure to benzene of one month, a decrease in the number of blood cells of 8–15% was observed for the lowest exposure concentration (< 1 ppm); for the highest concentration (≥ 10 ppm), this decrease was 15–36%. The haemoglobin concentration also decreased, but only for the group exposed to the highest benzene concentration (≥ 10 ppm). A small decrease was observed in a group of workers exposed to benzene concentrations of less than 1 ppm for the previous year.

In contrast, studies on United States petrochemical workers found no association between exposures to low levels of benzene and the development of haematotoxicity *(143–149)*. The studies were based on a review of 200 workers exposed to benzene concentrations of 0.01–1.4 ppm (0.03–4.55 mg/m^3) and 1200 employees working in the petrochemical industry for whom the mean 8-hour time-weighted average of benzene exposure was 0.6 ppm (1.95 mg/m^3) between 1977 and 1988 and 0.14 ppm (0.45 mg/m^3) between 1988 and 2002.

Thus, the haematological effects reported for benzene exposure concentrations of less than 1 ppm (3.25 mg/m^3) are controversial. In a recent review of benzene toxicity *(1)*, it was suggested that the differences in results between the studies in Chinese and United States workers might be due to differences in patterns of exposure or, alternatively, to the fact that the Chinese studies were purposely designed to test the effects of low-level benzene exposure and were thus superior

in their exposure assessment and timing of biological sampling in relation to exposure.

Immunological effects. Exposure to benzene affects the humoral and cellular immune system. These effects were reported for occupational exposures.

Cellular immunity is affected by changes in circulating lymphocytes, leading to a global leukopenia *(135,136,141,142,150–155)*. The benzene levels in workplace air ranged from 1 to 1060 ppm. In one study, routine leukocyte counts conducted every three months on employees of a small-scale industry in China revealed leukopenia in workers exposed to as little as 0.69–140 ppm (mean 6 ppm) for an average of 5–6 years *(156)*.

Another indicator of the alteration of cellular immunity is the change in leukocyte alkaline phosphatase activity. Increased activity is an indicator of myelofibrosis and is associated with both decreased white blood cell counts and with changes in bone marrow activity. Songnian et al. *(157)* showed an increase in the activity of this enzyme in benzene workers chronically exposed to about 31 ppm. This type of effect is confirmed by animal studies *(89,158–161)*.

Carcinogenic effects

Genotoxicity

The genotoxic effect of benzene has been shown to be mainly clastogenic rather than the induction of point mutations. Numerous studies have demonstrated that benzene and its primary metabolites cause chromosomal aberrations (hypodiploidy and hyperdiploidy, deletion and breaking) in humans after chronic exposure *(162–177)*. These chromosomal aberrations were observed in workers exposed to benzene concentrations high enough to induce dyscrasia. They are frequently localized in the peripheral blood lymphocytes and bone marrow. The main limitations of these studies lie in the lack of precise data concerning measurement of exposure, possible co-exposure to other substances and the absence of a suitable control group. Analysis of peripheral lymphocytes in workers exposed to benzene vapour (mean 30 ppm) revealed a significant increase in monosomy for chromosomes 5, 7 and 8, as well as an increase in trisomy or tetrasomy for chromosomes 1, 5, 7 and 8 *(176,177)*.

A significant increase in hyperploidy for chromosomes 8 and 21, along with an increase in translocations between chromosomes 8 and 21, have been observed in workers exposed to benzene at a mean concentration of 31 ppm (100.75 mg/m^3) *(173)*. Kim et al. *(178)* showed around a twofold increase in micronuclei and chromosomal aberrations. In contrast, studies showed a decreased level of t(14;18) chromosome translocation in workers *(179)*. Lichtman *(180)* did not find any chromosomal band damage.

The studies by Liu et al. *(118)* and Nilsson et al. *(119)* suggested that the metabolites of benzene activate oxygenated radical species, which can lead to DNA

changes and the formation of hydroxylated bases such as 8-hydroxy-2-deoxyguanosine. Navasumrit et al. *(181)* showed a significant twofold increase of leukocyte 8-hydroxy-2-deoxyguanosine and DNA strand breaks in temple workers. Buthbumrung et al. *(182)* reported a similar result in schoolchildren exposed to benzene.

The genotoxic capacities of benzene are due to its metabolites. Pandey et al. *(183)* showed with the micronucleus assay that metabolites of benzene, especially p-benzoquinone, produce significant DNA damage. Keretetse et al. *(184)* showed DNA damage with the comet assay. Galván et al. *(185)* showed that the WRN gene protects against DNA damage. For the first time, Shen et al. *(186)* reported an association between benzene exposure and increased mitochondrial DNA copy number.

Carcinogenesis

Animals. Chronic exposure of both rats and mice to benzene leads to an increased incidence of tumours, though mice are more sensitive *(100–102)*. The tumours formed include hepatomas, Zymbals gland tumours, lymphomas and tumours of the lung and ovary. However, there is no animal model for the induction of acute myeloid leukaemia, the major neoplastic lesion in humans. A study by Ross *(88,99)* in mice deficient in some detoxification enzymes showed that the genetically modified mice developed myeloid cell hyperplasia. Animal studies also showed that intermittent lifetime exposures to benzene at 980 mg/m^3 were more tumorigenic than short-term high-level exposures at 3900 mg/m^3 *(187)*.

Humans. Epidemiological studies have clearly demonstrated a causal relationship between exposure to benzene or solvents containing benzene in the workplace and the development of acute myeloid leukaemia *(123,124,188–191)*.

Rinsky et al. *(190)* studied a cohort of 1165 male workers employed in the Pliofilm[1] manufacturing industry between 1940 and 1965 up to 1981. The control data were the mortality data of American individuals of the same age as those studied in the cohort. An increase in mortality due to leukaemia was observed (9 cases observed instead of 2.7 expected), i.e. an SMR (standardized mortality ratio) of 3.37 (95% CI 1.54–6.41), along with an increase in mortality linked to multiple myeloma (4 cases observed, 1 case expected (SMR 4.09; 95% CI 1.10–10.47). The same evaluation repeated 15 years later reported a reduction in SMR for both leukaemia (SMR 2.56; 95% CI 1.43–4.22) and multiple myeloma (SMR 2.12; 95% CI 0.69–4.96) *(189)*. A significant increase in leukaemia, including myeloid leukaemia but not multiple myeloma, was observed with an increase in cu-

[1] Pliofilm is a trade name. It is a plastic, derived from rubber, that is impermeable to water and used to package or store equipment or food, for example.

mulative exposure to benzene (200 ppm-years,[2] i.e. 650 mg/m^3-years) *(190,192)*. An analysis of 4417 workers did not clearly reveal an increased risk of acute non-lymphocytic leukaemia, multiple myeloma or other types of lymphohaematopoietic cancers, with a low cumulative exposure to benzene, i.e. between 1 and 72 ppm-years (3.25 and 234 mg/m^3-years).

Kirkeleit et al. *(193)* performed a historical cohort study of workers employed in Norway's petroleum industry exposed to crude oil and other products containing benzene. Workers in the job category "upstream operator offshore", having the most extensive contact with crude oil, had an excess risk of haematological neoplasms (blood and bone marrow) (rate ratio (RR) 1.90; 95% CI 1.19–3.02). This was ascribed to an increased risk of acute myeloid leukaemia (RR 2.89; 95% CI 1.25–6.67) *(190)*. A peak exposure number of more than 100 ppm (325 mg/m^3) benzene over 40 days or more therefore appears to be a better indicator of the risk of leukaemia and multiple myeloma than long-term exposure to benzene *(194,195)*.

Within the most recently updated Pliofilm cohort, Paxton et al. *(196,197)* conducted an extended regression analysis with exposure description for the 15 leukaemia cases and 650 controls. They used all three exposure matrices, which gave estimates of 0.26–1.3 excess cancer cases among 1000 workers at a benzene exposure of 1 ppm (3.2 mg/m^3) for 40 years.

A study resulting from collaboration between the National Cancer Institute (NCI) and the Chinese Academy of Preventive Medicine (CAPM) analysed different types of haematopoietic disease, malignant or otherwise (development of the disease and mortality rate linked to the disease), in a cohort of 74 828 workers exposed to benzene. A group of 35 805 workers not exposed to benzene were used as a control. All the workers included in the study came from 672 factories in 12 Chinese cities *(189,198–201)*. The workers were employed from 1972 to 1987 for a mean duration of 12 years. A significant increase in the relative risk of haematological malignancies was observed (RR 2.6; 95% CI 1.4–4.7) as well as the risk for all leukaemias (RR 2.5; 95% CI 1.2–5.1), acute non-lymphocytic leukaemia (RR 3.0; 95% CI 1.0–8.9) and the combination of acute non-lymphocytic leukaemia and precursor myelodysplastic syndromes (RR 4.1; 95% CI 1.4–11.6) *(189)*. Analysis of these risks as a function of atmospheric benzene concentrations (< 10 ppm, 10–24 ppm and ≥ 25 ppm) or cumulative exposure to benzene per year (< 40 ppm-years, 40–99 ppm-years and ≥ 100 ppm-years) indicated that the risk for all haematological malignancies was increased significantly at benzene concentrations of less than 10 ppm (32.5 mg/m^3) and at cumulative benzene concentrations of less than 40 ppm-years (less than 130 mg/m^3-years). The risk of acute non-lymphocytic leukaemia and the combination of acute non-lymphocytic leukaemia and precursor myelodysplastic syndromes was significant

[2] Cumulative benzene exposure over a one-year period.

for a benzene concentration of between 10 and 24 ppm (32.5 and 78 mg/m^3) and for cumulative exposures of between 40 and 99 ppm-years (130 and 322 mg/m^3-years). Some criticisms may limit the utility of these data to develop a risk model. Limitations include the possibility of concurrent chemical exposures and a lack of reliable exposure data *(124)*.

Analysis of these results on the basis of exposure duration (< 5 years, 5–9 years and ≥ 10 years) demonstrated that the risk does not increase with exposure duration, irrespective of the disease studied. Analysis on the basis of different factories and sectors demonstrated that the risks are similar irrespective of the factory's activity, suggesting that the risks calculated are indeed attributed to benzene and not to other pollutants that may be found in the factories. A study conducted in workers employed in a shoe-making factory in Italy demonstrated the same results as the Chinese study *(202,203)*. The cohort was monitored from 1950 to 1999 and included 891 men and 796 women exposed to benzene concentrations of 0–92 ppm (0–299 mg/m^3). The cumulative mean exposure was 71.8 ppm-years (233 mg/m^3-years) for men and 43.4 ppm-years (141 mg/m^3-years) for women. A significant increase in the risk of leukaemia was observed in both sexes for the highest benzene concentration among the four concentration categories. This increase was more apparent in men. For cumulative exposures divided into the following four categories: < 40 ppm-years, 40–99 ppm-years, 100–199 ppm-years and > 200 ppm-years (<130, 130–322, 325–647 and > 650 mg/m^3-years), the SMR values for men were, respectively, 1.4 (95% CI 0.2–5), 3.7 (95% CI 0.1–20.6), 3.0 (95% CI 0.4–10.9) and 7.0 (95% CI 1.9–18.0). The type of leukaemia was not indicated.

A meta-analysis was conducted on 19 cohorts of workers in the petrochemical sector in the United Kingdom and the United States *(204)*. The overall cohort included 208 741 workers. Mean exposures and mean cumulative exposures to benzene, for the most exposed posts, were 1 ppm and 45 ppm-years (3.25 mg/m^3 and 233 mg/m^3-years), respectively. No increase in mortality due to acute myeloid leukaemia, chronic myeloid leukaemia, acute lymphocytic leukaemia and chronic lymphocytic leukaemia was observed in this study.

Recently, Richardson *(205)* evaluated data from a cohort of 1845 rubber hydrochloride workers. He reported an association between leukaemia mortality and benzene exposure at greatest magnitude in the 10 years immediately after exposure: RR 1.19 (95% CI 1.1–1.29). The association was smaller in the period 10–20 years after exposure.

Recent data indicate that benzene exposure is haematotoxic at less than 1 ppm. A decrease in circulating lymphocytes has been observed in workers exposed for six months to a mean exposure concentration of less than 1 ppm (3.25 mg/m^3) *(143–145)*. For leukaemia, the studies by Hayes et al. *(189,198,199)* and Yin et al. *(200,201)* in a cohort of approximately 75 000 workers and 36 000 controls indicated that the risk for acute myeloid leukaemia and precursor myelodysplastic

syndromes increased at between 10 and 24 ppm (32.5 and 78 mg/m^3) and, for cumulative exposures, between 40 and 99 ppm-years (130 and 322 mg/m^3-years).

The study by Rinsky et al. *(190)* described above demonstrates an increase in mortality related to the development of multiple myeloma in 1165 male workers followed up for one year. However, this result was not demonstrated in the other cohort studies *(200,201,203,206,207)*. A follow-up analysis by Rinsky et al. *(191)* indicated an increased but non-significant risk of multiple myeloma, with no evidence of an exposure–response relationship. In addition, case-control studies conducted in hospital populations indicate that exposure to benzene was probably not related to an increased risk of developing multiple myeloma *(208–213)*. Kirkeleit et al. *(193)* reported an increase in RR for multiple myeloma (RR 2.49; 95% CI 1.21–5.13) in workers exposed to crude oil and other products containing benzene employed in Norway's upstream petroleum industry.

The results of studies on non-Hodgkin's lymphoma appear to be less clear *(191,194,195)*. In a meta-analysis of 25 occupational cohorts, no association of non-Hodgkin's lymphoma was found *(207,214)*. A possible link between exposure to benzene and the development of non-Hodgkin's lymphoma was suggested by analysis of the results of the Chinese (NCI/CAPM) cohort described above *(189)*. The relative risk of mortality linked to non-Hodgkin's lymphoma in the overall cohort was 3 (95% CI 0.9–10.5). This increase was not statistically significant. However, the risk of non-Hodgkin's lymphoma increased significantly at the highest benzene concentration and for the longest exposure duration. For mean exposure to benzene concentrations < 10 ppm, 10–24 ppm and ≥ 25 ppm, the relative risks for non-Hodgkin's lymphoma were, respectively, 2.7 (95% CI 0.7–10.6), 1.7 (95% CI 0.3–10.2) and 4.7 (95% CI 1.2–18.1) ($P = 0.04$). For cumulative benzene exposures of < 40, 40–99 and ≥ 100 ppm-years, the relative risks for non-Hodgkin's lymphoma were, respectively, 3.3 (95% CI 0.8–13.1), 1.1 (95% CI 0.1–11.1) and 3.5 (95% CI 0.9–13.2) ($P = 0.02$). In addition, the risk of developing non-Hodgkin's lymphoma increases significantly with an increase in benzene exposure duration. The relative risks are, respectively, 0.7 (95% CI 0.1–7.2), 3.3 (95% CI 0.7–14.7) and 4.2 (95% CI 1.1–15.9) for workers exposed for less than 5 years, for between 5 and 9 years and for more than 10 years ($P = 0.01$). The other cohort studies did not reveal any positive relationship between exposure to benzene and an increase in mortality due to non-Hodgkin's lymphoma *(191,194,206)*. Kirkeleit et al. *(193)* reported no statistical differences between the groups in respect to non-Hodgkin's lymphoma.

Recently, Steinmaus et al. *(215)* conducted a meta-analysis of cohort and case-control studies of benzene exposure and non-Hodgkin's lymphoma and a meta-analysis of non-Hodgkin's lymphoma and refinery work. Results for the 22 studies indicated that the summary relative risk for non-Hodgkin's lymphoma was 1.22 (95% CI 1.02–1.47) ($P = 0.01$). When the authors excluded unexposed subjects in the "exposed group" (9 studies), the RR increased to 1.49. When studies based

solely on self-reported work history were excluded (7 studies), the RR rose to 2.12 (95% CI 1.11–4.02). In refinery workers, the summary RR for non-Hodgkin's lymphoma in all 21 studies was 1.21 (95% CI 1.00–1.46) ($P = 0.02$). When adjusted for the healthy worker effect, this RR estimate increased to 1.42 (95% CI 1.19–1.69). These results suggest that effects of benzene on non-Hodgkin's lymphoma might be missed in occupational studies if these biases are not accounted for.

In addition, a recent review by IARC concluded that there is limited evidence of an association between benzene exposure and acute lymphocytic leukaemia or non-Hodgkin's lymphoma *(216)*.

Table 1.1 collates studies on carcinogenic effects linked to human exposure to benzene, along with significant causal relationships between cancer and benzene exposure (subchronic and chronic).

In conclusion, the different studies available (in humans, in animals and in vitro) have demonstrated that benzene metabolites trigger chromosomal aberrations (translocation, monosomy, trisomy). The carcinogenic mechanism of action of benzene is linked to its genotoxic effects and the critical health outcomes are blood dyscrasias and leukaemia, particularly acute myeloid leukaemia.

Health risk evaluation

Critical health outcomes

Inhalation is the dominant route of exposure in humans. Inhaled benzene at concentrations found indoors is rapidly absorbed and distributed throughout the body. Benzene is rapidly metabolized in the liver and bone marrow to bipolar metabolites, which are responsible for its toxicity through clastogenic activity on DNA.

The critical health outcomes are blood dyscrasias and leukaemia, particularly acute myeloid leukaemia. The evidence is sufficient to conclude that a causal relationship exists between benzene exposure and both types of health effect observed. In addition, based on a recent review by IARC, there is limited evidence of an association between exposure to benzene with acute lymphocytic leukaemia and non-Hodgkin's lymphoma. Haematotoxicity is a risk factor for leukaemia *(108)*. This has been observed in many epidemiological studies in many countries. The studies were completed in occupational settings. A decrease in circulating lymphocytes has been observed in workers exposed for six months to a mean exposure concentration of less than 1 ppm (3.25 mg/m^3) *(143–145)*.

The association of benzene exposure with leukaemia was shown in studies of a cohort of male workers employed in the Pliofilm manufacturing industry between 1940 and 1965 *(190,217–219)*. These studies were updated by Paxton et al. *(196,197)* and confirmed the association of benzene exposure with the development of myelogenous leukaemia. Later studies by Hayes et al. *(189,198,199)* and Yin et al. *(200,201)* in a cohort of approximately 75 000 Chinese workers and 36 000 controls indicated that the risk for acute myeloid leukaemia and precur-

sor myelodysplastic syndromes increased at between 10 and 24 ppm (32.5 and 78 mg/m^3) and for cumulative exposures at between 40 and 99 ppm-years (130 and 322 mg/m^3-years).

In considering the exposure–response relationship, while there may be thresholds for these responses (blood dyscrasias and acute myeloid leukaemia) in individuals, there is no evidence of thresholds in population responses. Sensitive subpopulations have been found in which individuals have metabolic polymorphisms consisting of fast CYP2E1 oxidation activity or deficiencies in detoxification enzymes such as NQO1, or both. As regards the shape of the models describing the exposure–response relationship, Crump *(220)* found that multiplicative risk models described the data better than additive risk models and cumulative exposures better than weighted exposures. Crump *(220)* suggested that concentration-dependent non-linear models were more suited than linear models. Nevertheless, although there are biological arguments to support the use of concentration-dependent models, these results are only preliminary and need to be further developed and peer-reviewed.

Health relevance of indoor air exposures

Indoor concentrations of benzene are commonly higher than concentrations in outdoor air *(9)* as a consequence of the entry of benzene from outdoor sources (such as heavy traffic, petrol stations or industrial sites) and the presence of dominant benzene sources indoors. Indoor sources of benzene are mainly due to ETS, solvent use, building materials, attached garages and various human activities. On the other hand, in some regions unvented heating or cooking are the dominant sources indoors.

Also, the relatively low rates of ventilation typically found in houses and offices prevent the rapid dispersal of airborne contaminants. In areas where cooking and heating are provided by open fires in poorly ventilated housing, indoor levels of contaminants, including benzene, may reach high levels.

Indoor levels of benzene in homes and offices without strong indoor sources (e.g. ETS or unvented kerosene cooking/heating stoves) are generally less than 15 μg/m^3 (24-hour average), which are well below any of the lowest levels showing evidence of adverse health effects in either epidemiological or animal studies. In areas with high levels of ETS (e.g. discotheques), peak levels of 200 μg/m^3 have been observed. Incense burning or the use of unvented heating or cooking with kerosene stoves can drive peak indoor levels up in the 100–200 μg/m^3 range, with 24-hour levels in the range of 10–50 μg/m^3.

Conclusions of other reviews

IARC *(123,126)* classifies benzene as a known human carcinogen (Group 1). The USEPA lists benzene as Group A, a known human carcinogen, and lists the cancer risk for lifetime exposure to 1 μg/m^3 of benzene as 2.2–7.8 in a million

Table 1.1. Review of SMR and RR values identified in the literature for chronic human exposure to benzene (occupational and environmental studies) for carcinogenic effects

Reference	Exposure duration	Number and type of individuals exposed
Aksoy et al. *(146,147)* Retrospective study of workers exposed during the production of shoes, handbags and derived products between 1950 and 1965	1–28 years Mean exposure = 9.7 years	28 500 shoe industry workers in Turkey; controls: general population
Infante *(216,217)* Pliofilm cohort	1–10 years	748 workers; controls: general population
Rinsky et al. *(188,215)* Pliofilm cohort	1–14 years	1165 workers; controls: general population
Paci et al. *(201)* Retrospective study of workers in Florence employed from 1939 to 1984		
Yin et al. *(198,199)* Retrospective study of workers exposed in 233 paint, shoe, rubber and leather factories in China	More than 1 year	28 460 workers; 28 257 controls (workers not exposed in 83 factories)

Effect taken into account and measured	Concentration (1 ppm = 3.25 µg/m³)	Statistically significant association between effects measured and exposure
Mortality due to aplastic anaemia and acute leukaemia	150–210 ppm for 1–28 years Peak: 210–640 ppm	Positive association at all concentrations
Mortality due to myeloid leukaemia	Categories of exposure: < 40 ppm-years; 40–199 ppm-years; 200–400 ppm-years; > 400 ppm-years	Increase of standardized mortality rates in all categories with clear exposure–response trend
Mortality due to leukaemia	Total 1–39 ppm-years 40–199 ppm-years 200–399 ppm-years > 400 ppm-years	No significant association No association No significant association Positive association Positive association
Mortality due to lymphatic and haematopoietic tumours	Total	No association
Mortality due to multiple myeloma	Total < 40 ppm-years > 40 ppm-years	Positive association Positive association Positive association
Mortality due to aplastic anaemia	Exposure level not reported, exposure for ≥ 29 years	Positive association
Mortality due to leukaemia		Positive association
Mortality due to leukaemia	From 2 to 345 ppm (samples)	Positive association at all concentrations
Mortality due to lung cancer	From 2 to 345 ppm (samples)	Positive association at all concentrations

Reference	Exposure duration	Number and type of individuals exposed
Hayes et al. *(185)* Follow-up of the retrospective study of workers exposed to benzene in factories in 12 Chinese cities	Mean exposure duration = 12 years	74 828 workers; 25 805 controls
Ireland et al. *(193)* Study of chemical factory workers in the United States with a low degree of exposure to benzene		4127 workers; controls: general population
Kirkeleit et al. *(191)*	22 years	27 919 offshore oil workers ; 366 114 general working population matched by age, gender and place of residence
Steinmaus et al. *(213)*		Meta-analysis of 22 studies of benzene exposure and 21 studies of refinery workers
Richardson *(203)*	Up to 25 years	1845 rubber hydrochloride workers

Effect taken into account and measured	Concentration (1 ppm = 3.25 µg/m³)	Statistically significant association between effects measured and exposure
Development of all haematological cancers	< 40 ppm-years	Positive association
	40–99 ppm-years	Positive association
	≥ 100 ppm-years	Positive association
Development of leukaemia	< 40 ppm-years	No significant association
	40–99 ppm-years	Positive association
	≥ 100 ppm-years	Positive association
Development of non-Hodgkin's lymphoma	40 ppm-years	No significant association
	40–99 ppm-years	No significant association
	≥ 100 ppm-years	No significant association
Development of acute non-lymphocytic leukaemia	< 40 ppm-years	No significant association
	40–99 ppm-years	Positive association
	≥ 100 ppm-years	Positive association
Combination of myeloblastic syndromes and acute non-lymphocytic anaemia (development)	< 40 ppm-years	No significant association
	40–99 ppm-years	Positive association
	≥ 100 ppm-years	Positive association
Mortality due to leukaemia	0.5 ppm-years	No significant association
	3.5 ppm-years	No significant association
	12 ppm-years	Positive association
Acute myeloid leukaemia	Exposure classified by job description	Positive association
Multiple myeloma	Exposure classified by job description	Positive association
Non-Hodgkin's lymphoma	Exposure classified by job description	No significant association
Non-Hodgkin's lymphoma	"High" exposures (see paper for definition)	Positive association in both benzene and refinery workers
Age and temporal association between benzene exposure and leukaemia mortality	10 years since exposure (35–144 ppm-years)	Greatest association; RR 1.19; CI 1.10–1.29
	10–20 years since exposure	Smaller association; RR 1.05; CI 0.97–1.13
	> 20 years since exposure	No significant association

(124,221). The California Environmental Protection Agency lists the unit cancer risk for the same exposure as 29 in a million.

Guidelines

Guidelines on exposure levels are needed for indoor air because indoor air is a significant source of benzene exposure and inhalation is the main pathway of human exposure to benzene. Benzene is present in both outdoor and indoor air. However, indoor concentrations are generally higher than concentrations in outdoor air owing to the infiltration of benzene present in outdoor air and to the existence of many other indoor sources. Typically, indoor concentrations are below the lowest levels showing evidence of adverse health effects. Considering benzene is present indoors and taking into account personal exposure patterns, which are predominantly indoors, indoor guidelines for exposure are needed.

Benzene is a genotoxic carcinogen in humans and no safe level of exposure can be recommended. The risk of toxicity from inhaled benzene would be the same whether the exposure were indoors or outdoors. Thus there is no reason that the guidelines for indoor air should differ from ambient air guidelines.

Previous WHO benzene guidelines for ambient air were calculated using the Pliofilm cohort studies *(220)*. Since these studies, new data have become available, such as those on the large Chinese workers cohort *(189)*. However, the unit risks and risk assessment analysis based on these data are still not available. Hence we recommend continuing to use the same unit risk factors calculated from the Pliofilm cohort studies. The geometric mean of the range of the estimates of the excess lifetime risk of leukaemia at an air concentration of 1 $\mu g/m^3$ is 6×10^{-6}. The concentrations of airborne benzene associated with an excess lifetime risk of 1/10 000, 1/100 000 and 1/1000 000 are 17, 1.7 and 0.17 $\mu g/m^3$, respectively.

As noted above, there is no known exposure threshold for the risks of benzene exposure. Therefore, from a practical standpoint, it is expedient to reduce indoor exposure levels to as low as possible. This will require reducing or eliminating human activities that release benzene, such as smoking tobacco, using solvents for hobbies or cleaning, or using building materials that off-gas benzene. Adequate ventilation methods will depend on the site of the building. In modern buildings located near heavy traffic or other major outdoor sources of benzene, inlets for fresh air should be located at the least polluted side of the building.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome(s) for guideline definition

- Acute myeloid leukaemia (sufficient evidence on causality).
- Genotoxicity *(162–178,181–184,186)*.

Source of exposure–effect evidence

Occupational cohort study of male workers employed in Pliofilm manufacturing industry in China *(190–192,196,197,217–220)*.

Supporting evidence

Occupational cohort studies in China *(189,198–201)*, Italy *(202,203)*, Norway *(193)*, United States *(194,195,205)*.

Results of other reviews

- IARC: Group I (known human carcinogen) *(123,126)*.
- USEPA: Group A (known human carcinogen); the cancer risk for lifetime exposure to 1 μg/m^3 benzene is 2.2–7.8 in a million *(124,221)*.

Guidelines

- No safe level of exposure can be recommended.
- Unit risk of leukaemia per 1 μg/m^3 air concentration is 6×10^{-6}.
- The concentrations of airborne benzene associated with an excess lifetime risk of 1/10 000, 1/100 000 and 1/1000 000 are 17, 1.7 and 0.17 μg/m^3, respectively.

Comments

No change in the guideline as compared to *Air quality guidelines for Europe (2)*.

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2. Carbon monoxide

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General description

Carbon monoxide (CO) is a colourless, non-irritant, odourless and tasteless toxic gas. It is produced by the incomplete combustion of carbonaceous fuels such as wood, petrol, coal, natural gas and kerosene. Its molecular weight is 28.01 g/mol, melting point –205.1 °C, boiling point (at 760 mmHg) –191.5 °C (–312.7 °F), density 1.250 kg/m^3 at 0 °C and 1 atm and 1.145 kg/m^3 at 25 °C and 1 atm, and relative density (air = 1) 0.967 *(1,2)*. Its solubility in water at 1 atm is 3.54 ml/100 ml at 0 °C, 2.14 ml/100 ml at 25 °C and 1.83 ml/100 ml at 37 °C.

The molecular weight of carbon monoxide is similar to that of air (28.01 vs approximately 29). It mixes freely with air in any proportion and moves with air via bulk transport. It is combustible, may serve as a fuel source and can form explosive mixtures with air. It reacts vigorously with oxygen, acetylene, chlorine, fluorine and nitrous oxide. Carbon monoxide is not detectible by humans either by sight, taste or smell. It is only slightly soluble in water, blood serum and plasma; in the human body, it reacts with haemoglobin to form carboxyhaemoglobin (COHb).

The relationship of carbon monoxide exposure and the COHb concentration in blood can be modelled using the differential Coburn-Forster-Kane equation *(3)*, which provides a good approximation to the COHb level at a steady level of inhaled exogenous carbon monoxide.

Conversion factors

At 760 mmHg and 20 °C, 1ppm = 1.165 mg/m^3 and 1 mg/m^3 = 0.858 ppm; at 25 °C, 1 ppm = 1.145 mg/m^3 and 1 mg/m^3 = 0.873 ppm.

Indoor sources

Inhalation is the only exogenous exposure route for carbon monoxide. Anthropogenic emissions are responsible for about two thirds of the carbon monoxide in the atmosphere and natural emissions account for the remaining one third. Small amounts are also produced endogenously in the human body *(4,5)*. Exposure to low levels of carbon monoxide can occur outdoors near roads, as it is also produced by the exhaust of petrol- and diesel-powered motor vehicles. Parking areas can also be a source of carbon monoxide *(6)*.

Carbon monoxide is produced indoors by combustion sources (cooking and heating) and is also introduced through the infiltration of carbon monoxide from outdoor air into the indoor environment *(7)*. In developed countries, the most important source of exposure to carbon monoxide in indoor air is emissions from faulty, incorrectly installed, poorly maintained or poorly ventilated cooking or heating appliances that burn fossil fuels. In homes in developing countries, the burning of biomass fuels and tobacco smoke are the most important sources of exposure to carbon monoxide. Clogged chimneys, wood-burning fireplaces, decorative fireplaces, gas burners and supplementary heaters without properly working safety features could vent carbon monoxide into indoor spaces. Incomplete oxidation during combustion may cause high concentrations of carbon monoxide in indoor air. Tobacco smoke can be a major source of indoor exposure, as can exhaust from motor vehicles operating in attached garages *(6)*.

Combustion of low-grade solid fuel and biofuels in a small stove or fireplace can generate high carbon monoxide emissions, which may become lethal to occupants unless the flue gases are vented outdoors via a chimney throughout the entire combustion process. At the beginning of combustion, the pollutants released are dominated by particulate matter (elemental and organic carbon) but carbon monoxide dominates towards the end. Combustion of high-grade fuels such as natural gas, butane or propane usually produces much less carbon monoxide, provided that sufficient air is supplied to ensure complete combustion. Nevertheless, even devices using such fuels can cause lethal carbon monoxide intoxication if they are not properly maintained or vented or if air : fuel ratios are not properly adjusted.

Table 2.1. Indoor concentrations of carbon monoxide and indoor : outdoor (I : O) ratios

Study	Location	AM (SD) (mg/m^3)	GM (SD) (mg/m^3)	Median (mg/m^3)
Europe				
Maroni et al. *(9)*	Athens	1.3		
Georgoulis et al. *(10)*	Athens		4	
Chaloulakou et al. *(11)*	Athens	3.7		
Maroni et al. *(9)*	Basel	2.0		
Alm et al. *(12)*	Helsinki	2.1	1.6 (2.3)	1.8
Maroni et al. *(9)*	Helsinki	1.2		
Georgoulis et al. *(10)*	Helsinki	1.2		
Scotto di Marco et al. *(13)*	Helsinki	9.0	5.7	
		7.1	5.3	
		5.7	3.7	
		4.3	3.3	
		2.6	2.1	
		2.0	1.8	

Note: AM = arithmetic mean; GM = geometric mean; SD = standard deviation.

Incense burning in homes and public buildings such as stores and shopping malls can be a source of exposure to carbon monoxide. Jetter et al. *(8)* reported emission rates of 23 different types of incense, such as rope, cones, sticks, rocks and powder, that are typically used indoors. The measured emission rates of carbon monoxide ranged from 144 to 531 mg/hour. The authors estimated a peak concentration of 9.6 mg/m^3 caused by incense burning and therefore concluded that carbon monoxide concentrations could exceed the USEPA's National Ambient Air Quality Standard of 10 mg/m^3 for an 8-hour average, depending on the room volume, ventilation rate and the amount of incense burned. Incense burning might be a significant contributor to carbon monoxide exposure in cultures where incense is burned frequently, for example in religious rituals.

Indoor levels and relationship with outdoor levels

Results of recent studies on carbon monoxide concentrations in indoor air are summarized in Table 2.1. The studies are listed by continent. Studies concerning accidental or peak exposures are presented separately in Table 2.2. Representativeness and data quality, as well as the form in which the data are presented, vary greatly between the studies and make detailed comparisons meaningless except when comparing data within the same study. The general levels of carbon monoxide, however, vary so much between the locations and studies that patterns are easily discernible.

In the absence of indoor sources, current concentrations of carbon monoxide in indoor air in European and North American cities are well below the levels of existing air quality guidelines and standards. In the 1950s and 1960s, carbon

Range (mg/m^3)	I : O ratio (range)	Sources	Other information	Averaging time
		Smoking	Homes	
			Offices	1-hour
		Ambient air, gas stoves and ETS	Personal 24-hour exposures of children	
			Homes	
		Non-ETS	Exposure	
		ETS		Max. 15-minute
		Non-ETS		
		ETS		Max. 1-hour
		Non-ETS		
		ETS		Max. 8-hour
		Non-ETS		

Study	Location	AM (SD) (mg/m³)	GM (SD) (mg/m³)	Median (mg/m³)
Maroni et al. *(9)*	Prague	0.6		
Pan et al. *(14)*	Anhui			
Maroni et al. *(9,15)*	Milan	2.4		
Bruinen de Bruin et al. *(16)*		1.8 (1.3)	1.4 (2.2)	
		2.4 (1.5)	1.9 (1.9)	
		2.9 (1.6)	2.4 (1.8)	
		3.4 (2.2)	2.8 (1.9)	
		1.9 (1.7)	1.4 (2.2)	
		1.6 (1.2)	1.2 (2.0)	
		2.5 (2.2)	1.8 (2.4)	
		6.5 (2.5)	6.2 (1.4)	
		3.5 (2.9)	2.8 (1.9)	
Valerio et al. *(17)*				
Maroni et al. *(18)*	Italy	12–23		
Ross *(19)*	United Kingdom			
Raw et al. *(20,21)*	United Kingdom		0.4	
			0.3	
			0.8	
			0.9	
			0.7	
			0.4	
			0.3	
			0.4	
			0.5	
			0.7	
	(spring)		0.3	
	(summer)		0.2	
	(autumn)		0.5	
	(winter)		0.5	
Ditmitroulopoulou et al. *(22)*	London	1.9		
		2.3		
		2.0		
Milner et al. *(23)*	London			
Lai et al. *(24)*	Oxford	1.1	0.5 (3.9)	
			1.0 (2.3)	
Akland et al. *(25)*		0.5 (1.6)		
		15.4 (18.1)		
		10.5 (9.3)		
		6.5 (7.7)		
		5.6 (6.5)		
		5.0 (7.1)		
		4.3 (4.4)		
		4.1 (4.2)		
		3.9 (4.8)		
		3.7 (5.6)		

Note: AM = arithmetic mean; GM = geometric mean; SD = standard deviation.

Range (mg/m^3)	I : O ratio (range)	Sources	Other information	Averaging time
1.6 – 3				
2.1–3.9		Gas cooking	Homes	
	0.85	None	Homes	
	0.89	Gas cooking	Homes	
	1.45	ETS	Homes	
	1.10	Gas cooking & ETS	Homes	
	1.0	None	Offices	
	1.0	ETS	Offices [a]	
	1.19	None	Other indoor	
	2.95	Gas cooking	Other indoor	
	2.19	ETS	Other indoor	
15 (peak)			Shops	8-hour
18 (peak)			Bars	8-hour
35 (peak)			Bars, restaurants	
0.2–2.7			Homes	
		All-electric homes	Home kitchen	
		Gas oven/cooking	Home kitchen	
		Unflued heater	Home kitchen	
		ETS	Bedroom	
		Non-ETS	Bedroom	
			Rural	
			Suburban	
			Urban	
			City centre	
			All homes	
			All homes	
			All homes	
			All homes	
– 2.7	1.1	Marylebone Road	Lounge	
– 7.6	1.4	Gas cooking	Kitchen	
– 3.6	1.2	Smoking	Kitchen	
0.05–0.6	0.2–4.1	Busy street	Office building, 15-minute averages	
		No smoking	Personal exposure	
		Smoking		
			Public garage	
			Service station / car repair shop	
			Repair shop	
			Shopping mall	
			Residential garage	
			Restaurant	
			Office	
			Sports arena, concert hall	
			Store	
			Health care facilities	

[a] Problem in the self-reported exposures in the offices analysed in Ref. 16.

Study	Location	AM (SD) (mg/m^3)	GM (SD) (mg/m^3)	Median (mg/m^3)
		2.5 (4.3)		
		2.5 (3.3)		
		2.3 (4.1)		
		1.9 (2.8)		
		1.8 (3.4)		
Junker et al. *(26)*	Switzerland	3.5		
Pennanen et al. *(27)*	Finland	20–33		
North America				
Kim et al. *(28)*	Toronto	1.4 (0.5)		1.3
Levesque et al. *(29)*	Quebec	2.5		
Central America				
Lee & Park *(30)*	Costa Rica	1.6		
Naeher et al. *(31)*	Guatemala	28.6		
Clark et al. *(32)*	Guatemala	11		10
		0.5		0.4
Australia				
Brown et al. *(33)*				
		<1.2–4.6		
		20		
		34		
Asia				
Fischer & Koshland *(34)*	China, rural village	4.2 (0.7)	2.6 (2.7)	2.9
Jin et al. *(35)*	China, Gansu	11.3		
	China, Guizhou	1.8		
	China, Inner Mongolia	7.3		
	China, Shaanxi	10.8		
Hui et al. *(36)*	China, Hong Kong SAR	1.0 (0.3)	0.4 (1.4)	
Jo et al. *(37)*	Korea, Daegu			
	(summer)	0.5 (0.4)		0.5
	(winter)	0.9 (0.5)		0.8
	(summer)	0.4 (0.5)		0.3
	(winter)	0.8 (0.6)		0.8
Kim et al. *(38)*	Seoul	2.09		
Lawrence et al. *(39)*	India	1.2 (0.4)		
		1.2 (0.3)		
		2.1 (0.4)		
Gupta et al. *(40)*	India, New Delhi			

Note: AM = arithmetic mean; GM = geometric mean; SD = standard deviation.

Range (mg/m³)	I : O ratio (range)	Sources	Other information	Averaging time
			Other public buildings Residence School Church	
5.2 (peak)			Concert hall	Event (5½ hours)
			Five indoor ice rinks	Max 1-hour
0.1–3.8	0.4–1.0		Personal 24-hour	
		Open fire	Kitchen	
9–13		Open fire	Kitchen	
0.2–5.5		*Plancha*	Kitchen	
		Unflued gas heaters Normal conditions Gas supply restricted Misaligned burner	Laboratory room chamber test	1-minute
5.0–26.8 (1-hour peak)			Kitchen	24-hour
6.9–15.7		LPG for cooking & heating	33 bed/living rooms	24- hour
1.6–2.0		Coal for cooking & heating	32 cooking/living rooms	24- hour
6.6–7.9		Biomass for cooking & heating	65 cooking/living/ bedrooms	24- hour
6.3–15.3		Coal & biomass for cooking; coal for heating	24 bedrooms	24- hour
0.2–2.1			Offices	
– 2.3	0.8		Low-floor residences	
– 1.6	1.0			
– 1.1	1.0		High-floor residences	
– 1.3	1.6			
	3.6		Rural homes	
	1.7		Urban homes	
	1.7		Roadside homes	
1.2–3.5			Airport authority building control tower – ground floor	

Table 2.2. Accidental or peak exposure studies

Study	Location	Mean (mg/m³)	Range (mg/m³)
WHO *(41,42)*			60–115 (peak)
IEH *(43)*	United Kingdom		10–182 (peak)
Lebret et al. *(44)*	United Kingdom		5–108 (peak) 3–56 (peak)
El Fadel et al. *(45)*	Beirut		26–140 (peak)
Ross *(19)*	United Kingdom		121 (peak) 6–49 (peak) 3.5–4 (peak) 60 (peak)
Hampson & Zmaeff *(46)*	United States, Virginia		COHb % 6.6–50
Salonen et al. *(47)*	Finland, ice rink	> 140	COHb % 8–24
Guo et al. *(48)*	China, Hong Kong SAR		8–16
Lee & Wang *(49)*	China, Hong Kong SAR		44 (peak) 5.7
Thomassen et al. *(50)*	Camping tent	21.5% COHb (2.4)	200–550
Weaver & Deru *(51)*	Hotels, motels and resorts		

monoxide levels in urban air often approached or even exceeded these reference values, but drastic reductions in emissions from space heating and traffic have substantially reduced anthropogenic emissions in spite of the growing size of cities and increasing traffic *(9,29)*.

The highest reported non-accidental carbon monoxide levels are observed in public or residential garages and in primitive kitchens when cooking with open fires (Guatemala). Aside from open-fire cooking with solid fuels, the most common sources for elevated carbon monoxide concentrations in indoor air are unvented gas appliances, tobacco smoking and proximity to busy traffic. The lowest concentrations are found in homes, churches and schools at some distance (> 500 metres) from busy traffic and with no indoor sources. Carbon monoxide intoxication can be caused by single or repetitively generated high short-term peaks, and carbon monoxide poisoning is the leading cause of death from poisoning (accidental and intentional).

Carbon monoxide is a relatively unreactive gas under ambient air conditions and is not absorbed by building materials or ventilation system filters. Therefore, in the absence of indoor carbon monoxide sources, the indoor air concentration is the same as the concentration of ventilated or infiltrating outdoor air. Under these conditions, the indoor : outdoor (I : O) carbon monoxide concentration ratio should be 1.0; in practice, however, measured I : O ratios vary for two reasons.

- The outdoor air carbon monoxide concentration at the point of measurement may be significantly higher or lower than the concentration at the point

Sources	Other information	Averaging time
	Underground car parks, enclosed ice rinks, etc; homes with gas appliances	Several hours
Gas stove with pilot light	Homes	Peak when using a grill
Gas appliances	Kitchen Kitchen	Max. 1-minute Max .1-hour
	Underground parking	30-minute
Faulty boiler Gas cooking All-electric homes	Homes Homes Homes Homes	1-minute
Portable electric generators	Case studies on carbon monoxide poisoning	
Ice resurfacing machine	Case study of a carbon monoxide poisoning (epidemiological study)	
Petrol-fuelled	Indoor ice skating rink	15-minute
Incense burning Propane-fuelled	Chamber tests	 15-minute
Kerosene cooking stove	Experiment	120-minute
Boilers, water heaters, generators	68 cases of carbon monoxide poisoning, 27 deaths 1989–2004	

of ventilation air intake. Consequently, even in the absence of any indoor sources, the 15-minute I : O for carbon monoxide varies from 0.2 to 4.1 and the daily I : O from 0.4 to 1.2.

- Normal indoor sources, gas appliances and tobacco smoking increase the I : O ratios.

Kinetics and metabolism

Carbon monoxide hypoxia

Since the time of Haldane *(52)*, it has been assumed that the effect of carbon monoxide exposure is due to hypoxic effects *(53)*. Carbon monoxide enters the body via inhalation and is diffused across the alveolar membrane with nearly the same ease as oxygen (O_2). Carbon monoxide is first dissolved in blood, but is quickly bound to haemoglobin (Hb) to form COHb, which is measured as the percentage of haemoglobin so bound. The binding of carbon monoxide to haemoglobin occurs with nearly the same speed and ease as with which oxygen binds to haemoglobin, although the bond for carbon monoxide is about 245 times as strong as that for oxygen *(54–56)*. Thus carbon monoxide competes equivocally with oxygen for haemoglobin binding sites but, unlike oxygen, which is quickly and easily dissociated from its haemoglobin bond, carbon monoxide remains bound for a much longer time. In this way, COHb continues to increase with continued exposure, leaving progressively less haemoglobin available for carrying oxygen. The result is arterial hypoxaemia. Another effect of COHb is to

increase the binding strength of oxygen to haemoglobin, thus making release of oxygen into tissue more difficult *(57)*. The latter effect is quantitatively described as a leftward shift in the oxyhaemoglobin dissociation curve, proportional to the COHb level *(58)*.

The endogenous formation of COHb has been described by Coburn, Forster & Kane *(3)*. The model has also been tested under a wide variety of carbon monoxide exposure conditions and found to predict COHb more accurately than empirical methods *(54,59–66)*.

The most important variables in the formation of COHb are the concentration and duration of carbon monoxide in inhaled air and the rate of alveolar ventilation *(67)*. Alveolar ventilation, largely determined by body energy expenditure (exercise), can vary over a wide range and is thus the major physiological determinant of the rate of COHb formation and elimination.

Carbon monoxide will also reduce the diffusion of oxygen into tissue via myoglobin by formation of carboxymyoglobin. The formation of carboxymyoglobin also acts as another sink for carbon monoxide. This process has been described by a multicompartmental physiological model *(68,69)*. The models estimate the effects of carboxymyoglobin formation on carbon monoxide uptake, but the effect of carboxymyoglobin on tissue function is not clear. It is probable that such effects become important only for high levels of carbon monoxide exposure *(70)*. Binding of carbon monoxide to other proteins (cytochrome P-450 and cytochrome oxidase) have also been demonstrated, but the dosimetry is unclear and the functional significance appears to be limited to high levels of carbon monoxide exposure *(70)*.

Dosimetric compensations for COHb

Carbon monoxide, in addition to being an environmental contaminant, is produced endogenously. Thus, it is not surprising that physiological mechanisms have evolved to compensate for its presence in mammalian blood and tissues. These compensatory mechanisms must be considered when calculating the tissue dosimetry. For acute exposures, as COHb increases, arterial blood flow to the brain increases proportionally. Thus, even though the blood oxygen contents are decreased, in normal people the increased volume of blood tends to keep the amount of oxygen delivered to the brain constant, preventing hypoxia *(71–74)*. These investigators have demonstrated that brain tissue metabolism remains constant as the COHb increases until it approaches 20%, implying that brain tissue hypoxia does not occur with lower COHb levels. Thus it is apparent that the increased compensatory flow is sufficient to account for the shift in the oxyhaemoglobin dissociation curve. This compensatory activity also occurs in neonates and fetuses *(73,74)*. For chronic exposures to carbon monoxide, red cell volume increases or plasma volume decreases *(70)*, thus increasing the amount of oxygen that can be delivered.

Non-hypoxic mechanisms

An accumulating body of evidence indicates that direct carbon monoxide exposure (not COHb) can produce a number of brain cellular events that could potentially lead to serious functional consequences (see the section on health effects below). The direct effect of carbon monoxide on tissue has not been demonstrated in vivo, although such effects have been inferred by the observation of tissue effects in exposures in vivo that are very similar to such effects found with in vitro preparations. It would appear that the presence of carbon monoxide in tissues from in vivo exposure would depend on carbon monoxide dissolved in blood, because it had not yet bound with haemoglobin or because there could be some level of dissociation due to chemical equilibrium reactions. The amount of such dissolved carbon monoxide and the diffusion into various tissues has not been described or modelled. Thus, the dosimetry for putative non-hypoxic effects of carbon monoxide exposure is not known. The amount of dissolved carbon monoxide in blood would seem to be highest for high-level carbon monoxide exposure.

Comprehensive dosimetry

The final dose for carbon-monoxide-induced hypoxic effects is thus seen to be some measure of tissue oxygenation. This is an inverse measure in the sense that, as tissue oxygen increases towards the normal, function improves. As shown above, tissue oxygenation is determined by (*a*) the blood oxygen content (inversely proportional to COHb level), (*b*) the ease of dissociation from blood to tissue (the oxyhaemoglobin dissociation curve), (*c*) the volume of blood delivered to tissue and (*d*) the ability of tissue to utilize the oxygen (tissue respiration). To these we must add the rate of oxygen utilization by the tissue. The final criterion of tissue function is the energy metabolism rate in the tissue.

The issue of dosimetry is complex, but there exist physiologically based mathematical models to estimate many of the above variables and thus to predict tissue function. They are not mathematically trivial, but with modern computation tools the necessary calculations are readily performed *(3,75)*. Many of these models have been combined into "whole-body" models, which hold much promise for estimating physiological function (http://physiology.umc.edu/themodelingworkshop/).

Exposure–response relationship

The information required for regulatory guidance setting is some measure of the biologically critical concentration and duration of carbon monoxide exposure in inhaled air. To estimate environmental guidelines that provide reasonable protection against adverse health effects, information is required about what tissue dose produces what health effects. Given this critical tissue dose, one can estimate the various environmental concentrations, subject characteristics and

subject activities that will produce the critical tissue dose. Thus for a specific environmental case of interest, mathematical simulations can be done to estimate protective regulatory decisions. Therefore, for each health effect of interest, critical tissue oxygenation must be known.

It might be argued that the critical tissue dose is obtained from experimental evidence in which environmental exposure is given in the first place. Experiments, however, are not usually good simulations of actual scenarios of interest. The purpose of the simulations is to be able to simulate any environment of interest without having direct experimental evidence. Unfortunately, in the absence of adequate dosimetric information, and therefore dosimetric models, simulation by models is not possible. Thus for non-hypoxic effects, it is frequently necessary to use less general evidence from empirical environmental data to make estimates of critical exposures. To preserve exposure data from experiments and literature reviews, it would seem to be important to report both COHb and exposure concentration and duration. This would potentially permit calculation of tissue dose for non-hypoxic tissue effects when the dosimetry models are developed. It should be kept in mind that the tissue dose and the eventual health effect are not necessarily contemporaneous. Delayed sequelae may occur and cumulative exposure may be needed to become effective. These are really questions of physiological mechanisms.

Health effects

Identification of studies

For the acute health effects, the literature search was conducted in the PubMed and Web of Science databases, searching the keywords carbon monoxide and health. A special search for behavioural and neurological effects used PubMed with the following keyword statement: ("carbon monoxide" OR CO) AND ("human behaviour" OR "nervous system" OR CNS OR sensory OR "human performance" OR vision OR hearing OR auditory) NOT co- NOT smoking. Similar search statements were used for physiological and mechanistic articles. From these searches, 952 articles were found and, from these, 52 were deemed relevant and used in the review. The references in each of the relevant articles were searched to find any other articles that might have been missed by the automated searches.

A similar strategy was followed for a review of the health effects of chronic exposure. From these articles, 101 were deemed relevant and were used.

Chronic exposure

Definition of the health outcome

This review will discuss concisely and briefly human exposure to carbon monoxide in enclosed (i.e. closed) breathing spaces. Since outdoor air inevitably becomes indoor air, some consideration of carbon monoxide levels in outdoor air

and their effects on humans are required. To that end, there will be some discussion of epidemiological studies involving ultra-low-level carbon monoxide found in outside air. Exposure to high, potentially lethal levels are not considered here at any length and "delayed effects" are not examined because neither would be seen in indoor carbon monoxide exposure situations under normal circumstances. Because animal studies cannot at present provide much useful data about many aspects of the carbon monoxide poisoning syndrome *(76)*, they have been considered only in order to understand basic mechanisms by which carbon monoxide may impair human health.

This review extends the discussion of those issues involving carbon monoxide exposure in humans summarized in the 1999 WHO and 2005 European Union reports *(77,78)*. There has been no major attempt to recapitulate the review of most studies before roughly 1999. Other recent reviews on carbon monoxide exposure are available in monographs by Penney *(79–81)* and Kleinman *(6)*. Recourse to these works is strongly encouraged.

Tikuisis *(82)* reviewed human carbon monoxide uptake and elimination in 1996. Chen & Wang *(83)* reviewed the health effects of carbon monoxide in air pollution in major Chinese cities in 2000. Flachsbart *(84)* reviewed ambient and very low concentrations of carbon monoxide on humans more recently. Penney *(81)* recently reviewed pitfalls in making diagnoses of carbon monoxide poisoning, especially chronic poisoning. "Chronic" is defined as any exposure lasting more than 24 hours; "acute" is an exposure of 24 hours or less *(76)*.

Penney *(85)* reviewed the effects of carbon monoxide exposure on developing animals and humans in 1996. White *(86)* reviewed carbon monoxide poisoning in children in 2000. Public perceptions about carbon monoxide in the northern and southern regions of the United States, some relevant to indoor air, were investigated by Penney and published in 2008 *(87)*.

Penney reviewed the general characteristics of chronic carbon monoxide poisoning in humans in 2000 *(80)* and 2008 *(88)*, as did Hay et al. in 2000 *(89)* and Hay in 2008 *(90)*. In 2000,Greiner & Schwab *(91)* reviewed engineering aspects of carbon monoxide as it occurs in the living space.

Helfaer & Traystman *(71)* reviewed the cerebrovascular effects of carbon monoxide in 1996. In 2000, Hazucha *(92)* reviewed the effects of carbon monoxide on work and exercise capacity in humans. McGrath *(93)* reviewed the interacting effects on humans of altitude and carbon monoxide.

In 1996, Hiramatsu et al. *(94)* reviewed the impairment of learning and memory and neuronal dysfunction resulting from carbon monoxide exposure. In 2008, Hopkins *(95)* and Armstrong & Cunningham *(96)* reviewed the neurocognitive and affective outcomes of carbon monoxide poisoning in adults and children. Helffenstein *(97)* recently reported on a study investigating the neurocognitive and neurobehavioural sequelae of chronic carbon monoxide poisoning.

Early studies of chronic carbon monoxide poisoning

The early studies of Beck *(98,99)*, Lindgren *(100)*, Barrowcliff *(101)*, Wilson & Schaeffer *(102)*, Davies & Smith *(103)*, Trese et al. *(104)*, Kowalska *(105)*, Kirkpatrick *(106)*, Jensen et al. *(107)*, Ryan *(108)*, Tvedt & Kjuus *(109)*, Myers et al. *(110)* and Bayer et al. *(111)* on chronic carbon monoxide poisoning have been reviewed by Penney *(76)*. Other older studies, many coming out of the Second World War, have not been included in published reviews by this author. For example, Helminen *(112)* describes changes in the visual field caused by chronic coal gas (i.e. carbon monoxide) poisoning in 180 patients. The investigation was part of an extensive, systematic examination carried out at the First Medical Clinic of the University in Helsinki, Finland.

Sumari *(113)* describes the method used in Finland in examining victims of coal gas poisoning and the observations made in connection with it. The subject material comprises the results of the examination of 135 patients of which 71 are certain, "pure" chronic carbon monoxide cases. Of the cohort of 71, objective neurological symptoms were found in 60 cases. Out of 69 cases ophthalmologically examined, 66 gave positive results. Out of 65 cases oto-neurologically examined, the reaction of 52 was positive. In some cases the disease seemed to progress, although the patients being examined were then in surroundings free from coal gas.

Lumio, in an extensive 1948 study *(114)*, found fatigue, headache, vertigo, irritation, memory impairment, tinnitus and nausea to be the most frequent symptoms resulting from chronic carbon monoxide poisoning. Hearing disturbances were noted in 78.3% of the patients suffering from chronic carbon monoxide poisoning. A smaller number of hearing disturbances (26.7%) were found in patients exposed to carbon monoxide at work but in whom chronic carbon monoxide poisoning could not be confirmed. Thus, hearing disturbances were present in approximately three times as many patients suffering chronic carbon monoxide poisoning as in patients not affected. The majority of patients had a similar pattern of hearing deficiencies. The threshold of hearing was about normal at frequencies up to 1000 Hz. Hearing loss occurred above that frequency. This pattern of hearing deficiency was noted in 67.7% of patients who had suffered chronic carbon monoxide poisoning, but in only 14% of patients not so affected. Often, patients themselves were not aware of the presence of a hearing deficiency. Of those suffering from chronic carbon monoxide poisoning, 47.9% complained of hearing impairment during the time they were exposed to the carbon monoxide. The audiogram, however, showed changes in 78.3% of the patients with carbon monoxide poisoning. Follow-up examinations revealed that typical hearing losses improved only slightly or not at all. An improvement in hearing was found in only 26.7% of the cases, and it was always slight. The data suggest that typical hearing deficiency may appear during the initial stage of chronic carbon monoxide poisoning, when vestibular symptoms are not yet

present. For additional details see the Carbon Monoxide (CO) Headquarters web site (http://www.coheadquarters.com/ChronicCO/indexchronic2.htm).

Von Zenk *(115)* reported on rhino-cochlear-vestibular symptoms in 80 suspected cases of chronic carbon monoxide poisoning. The cochlear findings showed a perceptive disturbance with a high tone loss and largely retroganglionic damage. Subjective symptoms included vertigo that was accompanied by nystagmus more commonly in the confirmed group. There was also a diminution of the sense of smell.

Komatsu et al. *(116)* examined 733 workers at a steel-making facility. Mean ages of four groups broken out of the cohort was approximately 32 years (no significant difference). Group A1 was exposed to 58–291 mg/m^3, Group A2 to 70–1595 mg/m^3, Group B to < 23 mg/m^3 and Group C to < 12 mg/m^3 carbon monoxide in the course of their normal work. Median COHb saturation was 10–15% in Group A1, 20–25% in Group A2, 1–5% in Group B and 1–5% in Group C. The average frequency of health complaints was much higher for members of Groups A1 and A2 than for those of Groups B and C. A large variety of subjective health complaints were made by Group A1 and especially Group A2 members. For example, the highest frequency of complaints in reports included headache, poor hearing, chest pain, lassitude, fatigue and forgetfulness. A variety of objective health complaints were made by Group A1 and especially Group A2 members. The highest incidences, for example, included pallor, cardiac enlargement (cardiomegaly), coldness of the extremities and hyperactive patellar reflex. Average vital capacity was significantly less for members of Group A at any age than for members of Groups B or C. Average back strength was significantly less for members of Group A at age 30–40 years than for same-age members of Group C. The difference from members of Group B was very large and significant over the entire age range of the two groups.

Smith & Landaw *(117)* reported that smokers develop polycythaemia. Furthermore, smoking at increased elevation dramatically increases the extent of the polycythaemia. This, along with cardiomegaly, has been demonstrated numerous times following chronic carbon monoxide exposure in animals *(118,119)*.

Stern et al. *(120)* studied the effects of carbon monoxide exposure on deaths of New York City bridge and tunnel employees over the period 1952–1981. It was found that the tunnel workers experienced a 35% excess risk compared with the New York City general population; among the less exposed bridge workers the risk was not elevated. The elevated risk among the tunnel workers declined significantly within five years after ending occupational exposure, and there was also a significant decline after 1970, when a new ventilation system lowered carbon monoxide levels inside the tunnels and tunnel booths. The 24-hour average tunnel carbon monoxide concentrations were approximately 58 mg/m^3 in 1961 and 47 mg/m^3 in 1968. During periods of rush hour traffic in 1968, carbon monoxide concentrations in tunnel toll booths were as high as 76–192 mg/m^3.

Retrospective and case studies

Two questionnaire studies (A and B) of chronic carbon monoxide poisoning in North America have been reported by Penney *(76)*. A third questionnaire study (C) of 61 individuals sustaining chronic carbon monoxide poisoning was recently reported by Penney *(121)*. The large questionnaire study conducted in the United Kingdom in 1997 under the title "Carbon monoxide support" has been reviewed by Hay et al. *(89)*.

Two cases of chronic carbon monoxide poisoning in children *(122,123)* have been discussed by White *(86)* and another *(124)* by Hay *(90)*. Armstrong & Cunningham *(96)* report on three cases of chronic carbon monoxide poisoning in young children and the functional and developmental effects that resulted. A review of the effect of chronic or intermittent hypoxia on cognition in childhood *(125)* included carbon monoxide poisoning; it concluded that adverse effects have been noted at even mild levels of oxygen desaturation and that "studies of high-altitude and carbon monoxide poisoning provide evidence for causality".

Other studies looking at neuropsychological aspects of chronic carbon monoxide exposure such as those of Ryan *(108)*, Myers et al. *(110)*, Pinkston et al. *(126)*, Hartman *(127)* and Devine et al. *(128)* have recently been thoroughly reviewed by Helffenstein *(97)*. Helffenstein's findings from his own study of 21 people chronically exposed to carbon monoxide are detailed in that same 2008 source.

Ely et al. *(129)* describe 30 people who developed "warehouse workers' headache". COHb levels in the workers most exposed to exhaust gases were 21.1%. It is understood that this condition in the warehouse had continued for some time, making the exposure "chronic" rather than "acute". A majority of the people experienced acute difficulty with headache, dizziness, weakness, nausea and chest pain. Some complained of shortness of breath, vomiting, muscle cramps, difficulty in concentrating, visual changes and confusion. Follow-up symptoms present two years after the carbon monoxide exposure included numbness in the extremities, restlessness, persistent headaches, irritability, confusion, difficulty in walking or moving the extremities, and memory loss.

Walker *(130)* states that the incidence of chronic carbon monoxide exposure in Great Britain is officially 200 per year, while at the same time "250 000 gas appliances are condemned annually". He speculates that if only 10% of these appliances give off significant amounts of carbon monoxide that reach the breathing space of residents, as many as 25 000 people every year may be exposed to carbon monoxide in their homes. The carbon monoxide support study *(89)* found that "only one case out of 77 was correctly identified (i.e. diagnosed) on the basis of symptoms alone" and that medical professionals were the least likely group to "discover" the fact of the carbon monoxide poisoning.

Thyagarajan et al. *(131)* report on a 37-year-old woman chronically exposed to carbon monoxide for seven years. Her symptoms included seizure, persistent tiredness, problems with balance, headache associated with cognitive symptoms,

personality changes and depression. Magnetic resonance imaging of her brain five years after the end of carbon monoxide exposure showed a well-defined lesion in the globus pallidus, on the left. Hippocampal atrophy was also suggested. This case indicates that unilateral lesioning resulting from carbon monoxide poisoning can occur.

Prochop *(132)* reports on the case of four people chronically exposed to carbon monoxide in an apartment building in Florida as the result of a faulty gas heater. All four suffered transient loss of consciousness immediately prior to discovery of the problem. All four incurred cognitive impairments, while two also experienced residual coordinative deficits. Magnetic resonance imaging of the four people was said to be normal. One victim had an abnormal magnetic resonance spectroscopy scan.

Sari et al. *(133)* investigated an association between chronic carbon monoxide exposure and P-wave and QT interval characteristics of the electrocardiogram in 48 healthy male indoor barbecue workers and 51 age-matched healthy male controls. COHb in the two groups was 6.48% and 2.19%, respectively. Using Pearson analysis, there were significant correlations between COHb level and P-wave duration, maximum QT height, QT duration and corrected QT duration.

In a clinical review, Weaver *(134)* states that "lower level CO exposures can cause headache, malaise, and fatigue and can result in cognitive difficulties and personality changes". This assertion is borne out by Chambers et al. *(135)* (see Hopkins *(95)*), who prospectively followed 256 patients, 55 with "less severe" and 201 with "more severe" carbon monoxide poisoning. Less severe poisoning was defined as no loss of consciousness and a COHb level of ≤ 15%, while more severe poisoning was defined as loss of consciousness or a COHb of >15%. Of the less severely poisoned patients, 39% had cognitive deficits at six weeks. Of those more severely poisoned, 35% had cognitive deficits. In the less vs more severe groups, the incidence of depression was 21% and 16%, respectively, and that of anxiety was 30% and 11%, respectively. There was no difference in cognitive outcomes between the two groups. Interestingly, the prevalence of depression was higher in patients with the less compared with the more severe poisoning at six months. Likewise, the prevalence of anxiety was higher in patients with the less compared with the more severe poisoning at six weeks. These results suggest that loss of consciousness is not a requirement for carbon-monoxide-induced brain damage, and that carbon-monoxide-related cognitive (and other) outcomes may be independent of poisoning severity when that severity is based on COHb saturation.

In a recent clinical study, Keles et al. *(136)* characterized their patients as having acute carbon monoxide poisoning, when in actual fact most had chronic poisoning since the authors cite coal stoves and water heaters as carbon monoxide sources. These devices do not deteriorate overnight. Many studies do not characterize the exposure condition at all, or will characterize it as acute when in fact

Table 2.3. Summary data from five studies on chronic carbon monoxide poisoning

Study	Carbon monoxide (mg/m^3) AM (SD)	N1	COHb (%) AM (SD)	N2
Bayer et al. *(111)*	0–50 (estimated)	56	0.4–5.8	
Penney (A) *(76)*	497 (519)	15	9.65 (8.16)	11
Penney (B) *(76)*	257 (164)	25	9.0 (8.62)	29
Penney (C) *(121)*	174 (131)	23	9.2 (4.50)	12
Helffenstein *(97)*	143 (144)	14	14.5	2

Note: AM = arithmetic mean; SD = standard deviation.

it is chronic. The study found that COHb could not be used to rule out carbon monoxide poisoning. This has been known for some time, i.e. the poor relationship between COHb, symptoms and outcome. The most common symptoms they recorded were headache, nausea, dizziness and syncope.

Table 2.3 provides summary data from five studies on chronic carbon monoxide poisoning: Bayer et al. *(111)*, Penney *(76,121)* and Helffenstein *(97)*. N1 is the number of cases for which air carbon monoxide concentration data are available. N2 is the number of cases for which COHb data are available. It should be noted that, for all five studies, average COHb levels fall within the "less severe" carbon monoxide poisoning group as defined by Chambers et al. *(135)*.

Epidemiological studies

Epidemiological studies reported prior to 2000 dealing with carbon monoxide effects relative to mortality, birth weight, asthma, congestive heart failure, coronary artery disease, psychiatric admissions, etc. in humans have been reviewed by Penney *(76)*. The topic of congestive heart failure and environmental carbon monoxide levels was also reviewed by Morris *(137)*.

Mar et al. *(138)* evaluated the association between mortality in the elderly and air pollutants over a three-year period in Phoenix, Arizona. Total mortality was found to be significantly correlated with changes in ambient carbon monoxide and nitrogen dioxide, whereas cardiovascular mortality was significantly associated with carbon monoxide, nitrogen dioxide, sulfur dioxide, etc.

Moolgavkar *(139)* investigated non-accidental cardiovascular, cerebrovascular and chronic obstructive pulmonary disease deaths over eight years in three American metropolitan areas: two in California and one in Illinois. Carbon monoxide level was particularly found to have a stronger association with mortality than level of particulate matter. This association was noted to be stronger in Los Angeles County. This study is similar to an earlier epidemiological investigation by Hexter & Goldsmith *(140)*, reviewed by Penney *(76)*.

Hajat et al. *(141)* found a relationship between ambient carbon monoxide and asthma consultations for children in London. Sheppard et al. *(142)* examined the relationship between asthma and air carbon monoxide levels in Seattle for data

during the period 1987–1994. They found a 6% increase in the rate of hospital admissions for asthma related to carbon monoxide, with a three-day lag.

Yu et al. *(143)*, in another study in Seattle, found a 30% increase in asthma in children for a 1.2-mg/m^3 increment in carbon monoxide that lagged one day. They estimated 25% increases in the odds of increases in carbon monoxide, conditional on the previous day's asthma symptoms. It was concluded that there is an association between change in short-term air pollution levels and the occurrence of asthma symptoms among children in Seattle.

Karr et al. *(144)* analysed nearly 12 000 diagnoses of infant bronchiolitis between 1999 and 2002 in south-west British Columbia. They looked at infants' exposure within 10 km of home, and were able to account for confounding variables including sex, gestational age, maternal smoking and breastfeeding. An interquartile increase in exposure to nitric oxide, nitrogen dioxide, sulfur dioxide and carbon monoxide increased bronchiolitis risk by 8%, 12%, 4% and 13%, respectively. Infants living within 50 metres of a highway had an increased risk of 6%; those living in an area with higher exposure to wood smoke had an increase of 8% in their risk of bronchiolitis. Carbon monoxide posed the largest risk for bronchiolitis among the pollutants examined.

In studies by Hong et al. *(145,146)*, the occurrence of acute stroke mortality in Seoul is reported to be related to air pollution. Data covering 4- and 7-year periods were analysed. In the first study, stroke mortality increased 4.1% with a two-day lag. In the second study, a significantly increased risk of 1.06 (95% CI 1.02–1.09) was found for carbon monoxide, with a one-day lag. Nitrogen dioxide and ozone also appeared to play a role. This suggests, according to the authors, "an acute pathogenetic process in the cerebrovascular system induced by air pollution".

Yang et al. *(147)*, in a "case cross-over study" carried out on data for Kaohsiung (Taiwan, China), found that carbon monoxide and other air pollutants were significantly associated with increased numbers of admissions for cardiovascular diseases (CVD) on both warm and cool days. This study provides evidence that exposure to "higher levels of ambient contaminants, particularly carbon monoxide, increase the risk of hospital admissions for CVD".

Barnett et al. *(148)*, looking at data from Australia and New Zealand, found an association between outdoor air quality and cardiovascular hospital admissions. They found that for a 1-mg/m^3 increase in carbon monoxide, there were significant increases in hospital admissions of elderly people for total cardiovascular disease (2.2%), all cardiac disease (2.8%), cardiac failure (6.0%), ischemic heart disease (2.3%) and myocardial infarction (2.9%). In matched analyses, carbon monoxide had the most consistent association.

Bell et al. *(149)* studied hospital admissions for cardiovascular disease in 126 urban counties in the United States during 1999–2005. They found a positive and statistically significant association between same-day carbon monoxide exposure and increased risk of hospitalization for multiple cardiovascular outcomes

(ischemic heart disease, heart rhythm disturbances, heart failure, cerebrovascular disease and total cardiovascular disease). A 1.2-mg/m^3 increase in same-day daily 1-hour maximum carbon monoxide was associated with a 0.96% (95% CI 0.79–1.12) increase in risk of cardiovascular admissions.

In 1995, Morris et al. *(150)* reported an association between ambient carbon monoxide levels in seven United States cities and hospital admissions for congestive heart failure among elderly people, which showed a consistent association with daily variations in ambient carbon monoxide. This association was independent of season, temperature and other major gaseous pollutants. In 1997, Burnett et al. *(151)* found a similar association in ten Canadian cities. The logarithm of the daily high-hour ambient carbon monoxide concentration recorded on the day of admission displayed the strongest and most consistent association with hospital admission rates among the pollutants, after stratifying the time series by month of the year and simultaneously adjusting for temperature, dew point and the other ambient air pollutants. The relative risk for a change from 1.2 mg/m^3 to 3.5 mg/m^3, the 25th and 75th percentiles of the exposure distribution, was 1.065.

Yang *(152)* re-examined the reported association between air pollutant levels and hospital admissions for congestive heart failure in Taipei in 2008. The data examined covered the period 1996–2004. The number of admissions for congestive heart failure was significantly associated with the environmental presence of carbon monoxide and several other pollutants. Statistically significant positive effects on increased congestive heart failure admissions on cool days were observed only for the carbon monoxide levels.

Stieb et al. *(153)* conducted a study of nearly 400 000 emergency department visits to 14 hospitals in Canada between the early 1990s and the early 2000s. Twenty-four-hour averages of carbon monoxide and nitrogen dioxide exhibited the most consistent associations with cardiac conditions: 2.1% (95% CI 0.0–4.2) and 2.6% (95% CI 0.2–5.0) increase in visits, respectively, for myocardial infarction and angina per 0.8 mg/m^3 carbon monoxide. Thus, daily average concentrations of carbon monoxide and nitrogen dioxide exhibited the most consistent associations with emergency department visits for cardiac conditions.

Dales et al. *(154)* examined an association between air pollution and daily numbers of hospital admissions for headache in seven Chilean urban centres during the period 2001–2005. Relative risks for migraine associated with interquartile-range increases for carbon monoxide was 1.11 (95% CI 1.06–1.17) for a 1.3-mg/m^3 increase in carbon monoxide concentration. The authors concluded that air pollution increases the risk of headache in Santiago Province. There was no significant effect of modification by age, sex or season.

In a massive epidemiological study, Ritz & Yu *(155)* studied a cohort of 125 573 singleton children born in Los Angeles. Excluded were infants born before 37 or after 44 weeks of gestation, those weighing below 1000 or above 5500 grams at birth, those for whom fewer than 10 days of carbon monoxide measurements

were available during the last trimester, and those whose mothers suffered from hypertension, diabetes or uterine bleeding during pregnancy. Within the cohort, 2813 (2.2%) were low in birth weight (between 1000 and 2499 grams). Exposure to higher levels of ambient carbon monoxide (> 6.4 mg/m^3, 3-month average) during the last trimester was associated with a significantly increased risk for low birth weight (odds ratio (OR) 1.22; 95% CI 1.03–1.44) after adjustment for potential confounders, including commuting habits in the monitoring area, sex of the child, level of prenatal care, and the age, ethnicity and level of education of the mother. Levels of environmental carbon monoxide previously thought to be extremely low were shown to reduce birth weight in women exposed to carbon monoxide during the last trimester of pregnancy.

Maisonet et al. *(156)* followed the Los Angeles study with an investigation on birth weight in Boston, MA, Hartford, CT, Philadelphia, PA, Pittsburgh, PA, Springfield, IL and Washington, DC. Their results suggest that exposure to ambient carbon monoxide (and sulfur dioxide) increases the risk of low birth weight at term. This risk is increased by a unit rise in the average concentration of carbon monoxide in the third trimester.

Chen et al. *(157)* assessed the association between ambient air pollution and daily elementary school absenteeism in Washoe County, Nevada in the period 1996–1998. A total of 27 793 students were enrolled. The daily average absence rate was 5.09% (SD = 1.54%). The daily average carbon monoxide concentration was 3.2 mg/m^3. After adjustment for the effects of weather, day of the week, month, holidays and time trend, they found that carbon monoxide and oxygen were statistically significant predictors of daily absenteeism. For every 1.2-mg/m^3 increase in carbon monoxide concentration, absence increased by 3.79% (95% CI 1.04–6.55).

Two studies examining cardiovascular events and long-term exposure to carbon monoxide at ultra-low levels (i.e. 1.2–1.8 mg/m^3) found no significant association with changes in the carbon monoxide concentration in ambient air *(158,159)*.

Experimental studies

Past reviews of air quality mainly discuss acute studies of carbon monoxide exposure at lower concentrations. Even though hypoxic stress may have been the only underlying mechanism at work, some nonetheless reported positive effects. It can be argued that when considering exposure to air pollution in human residential and work environments, these studies have limited significance and model rather poorly human responses to long-term carbon monoxide exposure.

Symptomatology

Recognizing the onset of carbon monoxide poisoning is crucial, as it can be fatal in just a few minutes. The symptoms are usually non-specific and appear to

involve many of the body systems. Common symptoms include headache, lethargy/fatigue, nausea, dizziness and confusion. A victim may also suffer from shortness of breath, cardiac palpitations, convulsion, paralysis, loss of consciousness, coma and eventually death. Many reviews list the step-wise onset of various symptoms in acute carbon monoxide poisoning as they relate to blood COHb levels. However, the relationship in reality between blood carbon monoxide levels and symptomatology is extremely poor. There is no hyperventilation induced by carbon monoxide poisoning or increased salivation, taste/odour changes, eye watering or coughing, as are produced by carbon monoxide's toxic twin, hydrogen cyanide. Age, anaemia, increased elevation, cardiopulmonary disease and prior exposure to carbon monoxide can increase susceptibility to carbon monoxide toxicity. The median level of COHb in people dying of uncomplicated carbon monoxide poisoning is 53–55%.

An important key to identifying carbon monoxide poisoning is the victim's environment and immediate past living or work situation. Was the victim exposed to sources of carbon monoxide such as uncontrolled fires, motor vehicles, fuel-burning heaters or other internal combustion engines in a poorly ventilated enclosed space? Are others in that environment (e.g. family members or pets living in the same house) displaying similar symptoms? These facts are critical in accurately identifying carbon monoxide poisoning.

First and foremost, the victim must be moved out of the contaminated area into fresh air. Eventually, the carbon monoxide will be eliminated from the blood through normal ventilation, although often serious health damage may be done before this can occur, so emergency measures should be started immediately.

In 1895, John Scott Haldane demonstrated that rats survive carbon monoxide poisoning when placed in oxygen at two atmospheres pressure. In 1942, End & Long treated carbon monoxide poisoning in experimental animals with hyperbaric oxygen. The first human clinical use of hyperbaric oxygen therapy in carbon monoxide poisoning was by Smith & Sharp in 1960 *(80)*. This type of therapy is now recommended for most seriously, acutely poisoned victims, but there have been some studies that fail to show its efficacy *(81)*. If hyperbaric oxygen therapy is to be used, it must be initiated immediately (within 12 hours) on reaching a health care facility.

Pathophysiological mechanisms

Since the time of Haldane *(52)*, it has been presumed that the attachment of carbon monoxide to haemoglobin, thus preventing the carriage of adequate oxygen and the impaired release of oxygen from the remaining oxyhaemoglobin (i.e. hypoxic stress) was the major mechanism by which carbon monoxide exerts its health-damaging effects. At low COHb levels and in the presence of normal vasomotion and hyperaemia, it has been difficult to understand how carbon monoxide can cause immediate or long-term cellular, tissue and organ damage. Evi-

dence for various cellular mechanisms not requiring hypoxic stress has recently appeared. See also http://www.coheadquarters.com/coacute.mech1.htm.

Ischiropoulos et al. *(160)* found in rat studies that the potent oxidant species, peroxynitrite, was generated in the brain from nitric oxide and that a cascade of events could lead to "oxidative stress" in carbon monoxide poisoning. Thom & Ischiropoulos *(161)* reported that platelets released nitric oxide when incubated with carbon monoxide and that carbon monoxide concentrations as low as 12 mg/m^3 were capable of doing this in vitro. They concluded that carbon monoxide levels produced in vivo when humans are exposed to carbon monoxide "can cause endothelial cells to liberate nitric oxide and derived oxidants, and that these products can adversely affect cell physiology". Using microelectrodes in rats, it was seen that carbon monoxide exposure caused nitric oxide concentration to nearly double to 280 nM through the modulation of nitric oxide synthase *(162)*.

It was found that platelet activating factor was involved in the adherence of neutrophils to brain endothelium after carbon monoxide poisoning and that the process required nitric-oxide-derived oxidants *(163)*. Thom et al. *(164)* postulated that carbon monoxide poisoning causes "adduct formation between myelin basic protein (MBP) and malonylaldehyde, a reactive product of lipid peroxidation, resulting in an immunological cascade". It was found that carbon-monoxide-poisoned rats displayed impaired maze-learning that did not occur in similar rats made immunologically tolerant to MBP. They suggest that this mechanism may explain brain damage occurring days after treatment for carbon monoxide poisoning, and be the reason for the observed lack of a simple dose–response relationship between COHb level at presentation and outcome. The use of hyperbaric oxygen following carbon monoxide poisoning in rats prevented deficits in maze-learning performance and MBP immune-mediated neurological dysfunction *(165)*.

In blood obtained from 50 patients who had sustained carbon monoxide poisoning, platelet–neutrophil aggregates were detected and plasma myeloperoxidase concentration was elevated, suggesting that the processes seen in animals also operate in humans *(166)*.

Thus, recent studies suggest that the intracellular uptake of carbon monoxide could be a major cause of neurological damage (i.e. brain damage). When carbon monoxide binds to cytochrome oxidase, it causes mitochondrial dysfunction. The release of nitric oxide from platelets and endothelial cells inside blood vessels, forming the free radical peroxynitrite, further inactivates mitochondrial enzymes and damages the vascular endothelium of the brain. The end result is lipid peroxidation of the brain, which starts during recovery from carbon monoxide poisoning. With reperfusion of the brain, leukocyte adhesion and the subsequent release of destructive enzymes and excitatory amino acids amplify the initial oxidative injury. Such endovascular inflammation may be a major mechanism leading to organ dysfunction.

Other recent studies indicate that carbon monoxide poisoning can cause immune system dysfunction *(164)* that causes decrements in learning not observed in immunologically tolerant animals. This may be based on adduct formation between MBP and malonylaldehyde, a reactive product of lipid peroxidation, resulting in an immunological cascade. Thus, carbon monoxide poisoning appears to trigger immunological reactions, just as a number of other disease states do. Therefore, a third damaging mechanism of carbon monoxide exposure appears to be through its action on the immune system.

The information summarized above suggests that the damaging effects of carbon monoxide are not only due to its action in binding to haemoglobin and interfering with oxygen delivery, i.e. hypoxic stress. Although this process certainly takes place and is undoubtedly important in higher-level and acute carbon monoxide poisoning, other processes not previously known result in endothelial inflammation and immune activation, causing interference with blood flow and the destruction of cellular machinery. The operation of these pathways and their products explain the effects of carbon monoxide at very low air–carbon monoxide and COHb levels, and what occurs during extended exposure, and finally the seeming lack of a dose–response relationship between air–carbon monoxide concentration, COHb, immediate symptoms and the long-term health effects.

Acute exposure

Effects on exercise duration

There have been no reliable demonstrations of health effects due to acute carbon monoxide exposure in normal, healthy people where exposures resulted in COHb levels below 6%, except for limitation of maximal exercise duration. In laboratory experiments, people exposed to carbon monoxide before maximum exercise tests had reduced exercise duration *(167–172)*. The duration was reduced as an inverse function of COHb level. A linear equation was fitted to the data *(167)* but the equation should have been curvilinear. This is clear from inspection of the data because the zero COHb point, had it been included in the fitting, would have been plotted well below the intercept of the fitted curve. At higher COHb, however, the curve is nearly linear. An increase in COHb of 4.5% produced a drop in exercise time of about 30 seconds. In the Ekblom & Huot study *(167)*, the baseline mean exercise duration was about 5.2 minutes. Another metric of the effect magnitude was calculated by estimating the maximum total calories expended from the amount of work performed. Here, a 4.5% increase in COHb level reduced the maximum exercise from a total expenditure of about 112 kcal to some 90 kcal.

The exercise effect of carbon monoxide exposure in healthy subjects was produced by reduced oxygen delivery to the exercising muscle. At 20%, COHb reduced the arterial oxygen content from about 19.8% to about 15.8% by volume.

Normally, one would expect reduced oxygen dissociation from arterial blood into muscle tissue because of the shift in the dissociation curve, but in the case of exercising muscle the oxygen partial pressure of the tissue is likely to have been so low that the dissociation shift did not matter *(167)*.

Also, at maximum exercise, no further increase in blood flow to the muscle was possible. Thus, in this experiment, the only appreciable determinant of tissue oxygenation was the COHb. No account of the possible role of carboxymyoglobin was possible.

When laboratory maximal exercise testing was done with patients who exhibited stable angina pectoris due to coronary artery disease, the results were quite different from normal subjects *(173–178)*. Here the subjects were also given maximal exercise tests, but the criterion for stopping was not exhaustion but the onset of angina. Subjects were also exposed to lower levels of carbon monoxide, producing a maximum of nearly 6% COHb. In the baseline (no carbon monoxide) condition, the mean maximum exercise time was around 8.2 minutes. Allred et al. *(175)* showed that an increase in COHb of 4.5% reduced exercise time by 36 seconds and reduced total maximum energy expenditure from about 64 kcal to about 30 kcal. Thus it is seen that the magnitude of effect produced by an increase in COHb of 4.5% in not dramatically greater than for normal subjects. The difference is that the cardiac impairment has simply reduced the baseline exercise ability.

The angina patient's baseline exercise ability was reduced from a maximum energy expenditure of 112 kcal to 64 kcal by the inability of the heart to supply sufficient blood flow to provide oxygen to the exercising muscles. The further decrease in exercise time was due to the same mechanism as for normal subjects (reduced arterial content of the same magnitude), which produced nearly the same magnitude of effect. To be sure, the percentage exercise reduction is greater for the angina patients than for the normal subjects, but this is simply due to the reduction in baseline exercise ability.

It is not clear whether the slightly greater observed effect of COHb in the patients compared to the normal subjects would be considered statistically significant or physiologically meaningful. Another consideration in the angina data is the fact that COHb was not extended to higher levels as it was for normal subjects. Clearly, this was done for ethical reasons, but the possibility exists that higher exposures would have led to greater magnitudes of effect than for normal subjects.

It might be argued that the data on the effect of carbon monoxide exposure in angina patients contributes little additional information needed for regulatory decisions. However, heart disease is a leading cause of sickness and death worldwide, and it is plausible that coronary artery disease would make patients more susceptible to cardiac failure from increased hypoxic cardiac stress *(179)*, but there are no data to evaluate this hypothesis. On the other hand, individuals

with heart disease represent a large fraction of the population and therefore the angina studies do address an issue of public health concern.

Brain function effects

Clinical reports of symptoms of low-level acute carbon monoxide poisoning (headache and nausea) are commonly cited *(180)* for COHb levels of 10–20% but were not observed in a double-blind study for COHb levels below 20% *(181)*. Headache and nausea were reported in a double-blind study at COHb levels of 25–30% *(182)*.

A large number of behavioural studies were critically reviewed by Benignus *(183,184)* involving sensory, psychomotor, vigilance, cognitive and schedule-controlled behaviour in both humans and rats. Human studies were largely unreliable in the sense that they were not replicable, sometimes even by their original authors. Rat studies were highly consistent but demonstrated statistically significant effects only when COHb exceeded about 20%.

Benignus *(183)* meta-analysed the carbon monoxide literature, fitting dose–effect curves and attempting to relate the rat and human carbon monoxide data and the human hypoxia data. The rat carbon monoxide data were meta-analysed and the internal dose (oxygen delivery by arterial blood) was estimated. The extra behavioural effect of hypothermia (which results from COHb increase) was also estimated and subtracted. The internal dose for humans exposed to carbon monoxide was also calculated, but hypothermia (which does not occur in humans for the duration of acute exposures) was not considered. The internal dose for hypoxic hypoxia in humans was calculated, in addition to the hypocapnia (which occurs due to hyperventilation in hypoxic hypoxia but not carbon monoxide exposure). The carbon monoxide effects were corrected by subtracting the effects of hypocapnia. When all of the internal doses and the behaviourally corrected dose–effect curves were compared, they nearly overlay each other. The conclusion was that, when arterial oxygen content was used as the internal dose and extraneous effects were subtracted, the behavioural effects of carbon monoxide hypoxia and hypoxic hypoxia were of equal magnitude for humans and were equal in rate to the magnitude of carbon monoxide hypoxia. The results were expressed in equivalent of estimated COHb.

The above-mentioned dose–effect curves reached the 10% effective dose (ED-10) at mean COHb ~ 20%, with upper and lower 95% confidence limits of about 22.2% and 18.8% *(184)*. The ED-10 was selected as a point of interest because in the behavioural literature, and with the typical number of subjects, the ED-10 is about the magnitude of effect that becomes statistically significant or behaviourally important. A continuous non-linear function was fitted to the data and thus there is a continuum of magnitude of effect estimates, which may be used to estimate severity of effects between zero and about 30% COHb and higher by extrapolation from rats. It may not be inferred from these results that effects be-

low a COHb of 20% are absent; they gradually diminish towards zero at a COHb of zero.

These results provide an example of compensatory physiological action, i.e. the increased arterial blood flow to the brain sufficient to keep tissue oxygen supply nearly constant *(73,185)*. It was observed by these workers that brain energy metabolism remained statistically unchanged until COHb exceeded 20%, because up to that point blood flow could increase sufficiently to offset the carbon-monoxide-induced hypoxia. At COHb levels of around 30%, the brain metabolism fell precipitously. These physiological results agree almost exactly with the behavioural data.

It is interesting that small decreases in mean brain energy metabolism as well as in mean behaviour are estimated to occur below 20% COHb. This could be attributed to an actual small effect or to some small fraction of susceptible subjects having larger effects or to an inappropriate statistical model for the dose–effect curves. This is an area requiring additional study, since at the present stage of knowledge the question cannot be resolved.

An implication of the above analysis is that if, owing to some pre-existing cardiovascular or pulmonary disease, the compensatory increase in blood flow were impaired, small increases in COHb could produce larger decreases in tissue oxygen and thus larger behavioural effects. No data have been reported to test this hypothesis.

Compromised brain function, in addition to being an adverse effect in itself, can contribute to sensory impairment that could result in failure to detect signs of danger or could impair decision-making capabilities, leading to an inability to respond appropriately to danger. The ability to avoid or flee danger could also be impaired by carbon-monoxide-induced limitations on exercise. Such effects of acute exposure can potentially lead to consequences ranging from minor injuries to serious injuries and death. Behaviourally or physically impaired people exposed to carbon monoxide could also endanger others in their vicinity.

Quality of the exposure and effects measures

It has been customary to specify the "dose" of carbon monoxide as either the amount in blood as COHb or as the concentration in the inhaled air. The effects of carbon monoxide are, however, not strictly determined by either of these metrics. The health effects are a product of tissue functioning and these, in turn, are functions of some tissue dose metric. An effort is made below to specify tissue dosimetry where knowledge permits and to point to gaps in knowledge when appropriate.

Susceptible populations and effect modifiers

Any person with some form of impaired oxygen uptake and delivery would be more sensitive to the acute hypoxic effects of carbon monoxide exposure. Thus,

hypothetically, any cardiac, vascular or pulmonary disease would have such an effect, as would other factors that limit the blood's ability to transport oxygen, such as anaemia. Also, presumably, multiple diseases in a particular person could increase that individual's risk of greater effects; the potential interaction need not necessarily be simply additive. The severity of a given disease state would influence the maximum COHb, possibly before adverse effects became noticeable, and could determine the maximum amount of effort that could be expended. The magnitude of a carbon monoxide effect would depend on the amount of oxygen available for metabolism in the tissue under consideration. Because multiple cardiac, vascular and pulmonary diseases in one person are not uncommon, it would not be surprising if some impaired people were adversely affected by even small increases in COHb. No data are available to evaluate this conjecture, but quantitative physiological analyses to further delimit the range of effects would be possible.

Other possible sensitive groups are pregnant women, whose endogenous COHb is greater, and fetuses, whose haemoglobin has somewhat greater affinity to carbon monoxide than that of adults.

There are numerous situations in which carbon monoxide is not the only source of hypoxia. Until a person is adapted to high altitude, the resulting arterial hypoxia is directly additive (in terms of arterial oxygen content) to carbon monoxide hypoxia *(178)*, and the increased pulmonary ventilatory response also increases carbon monoxide uptake. Increased inhaled carbon dioxide increases pulmonary ventilation and thus carbon monoxide uptake. Hydrogen cyanide inhibits tissue respiration and thus adds to hypoxic effects, in addition to strongly stimulating increased pulmonary ventilation. These effects are of interest because all of the above pollutants are combustion products. These effects are enumerated in detail by Benignus *(184)* and physiological effects and interactions have also been quantitatively estimated in interesting cases by Benignus *(186)* using computerized mathematical models of physiological function. Thus, the presence of any or all of the above combustion gases would exacerbate the effects of carbon monoxide exposure.

The concomitant behaviour of people exposed to carbon monoxide can also make them more sensitive to its effects. Higher rates of physical exercise increase pulmonary ventilation, thereby increasing the COHb formation rate, and increase oxygen metabolism, exacerbating the hypoxia. Increased body temperature from external heat or inappropriate clothing would increase pulmonary ventilation. Those who are anxious owing to emotional or psychological conditions have increased pulmonary ventilation.

Clearly, impaired persons could be exposed to multiple hypoxic toxicants while engaged in situations in which pulmonary ventilation would be elevated. Even though the carbon monoxide in these environments might be insufficient to produce effects in controlled laboratory experiments, the real world is much

more complicated and the possibility of such complex multiple effects cannot be dismissed.

Health risk evaluation

There are several health concerns associated with exposure to carbon monoxide. The best understood health effects appear to be produced by hypoxia due to the binding of carbon monoxide to haemoglobin, which reduces the oxygen-carrying capacity of the blood as well as decreasing the dissociation of oxygen into extravascular tissue. COHb is widely used as a biomarker for carbon monoxide exposure. Carbon monoxide also binds with myoglobin and cytochrome oxidase and P-450, but the magnitude and the effects of such binding are less well explored.

High-level exposures (over several hundred mg/m^3) can cause unconsciousness and death. There can be severe and permanent CNS damage, even in cases where individuals do not experience loss of consciousness. Evidence is also mounting that carbon monoxide can produce a cascade of cellular events leading to adverse effects that are not necessarily ascribable to hypoxia (i.e. COHb may be a less reliable biomonitor for these effects).

Acute exposure

Acute laboratory exposure to carbon monoxide in healthy young people has been shown to decrease duration of maximum exercise tests in a COHb (dose)-related manner. The same phenomena were demonstrated in patients with stable angina, but only at a lower range of COHb. The latter effect is presumably due to limitation of heart oxygen supply because of an inability to increase blood flow in the presence of, for example, stenoses in the coronary arteries.

In early acute laboratory exposures of healthy young people, brain function (as measured by reduced behavioural performance) was reported to be impaired in a COHb-related manner when COHb ranged from 2.5% to around 10%. These studies were, however, not replicable in any case where such replication was attempted. It has been suggested, based on physiological analysis and extrapolation, that brain function should not be reduced by more than 10% until COHb approaches around 18%. With laboratory carbon monoxide exposures of a few hours' duration, no symptoms were reported, even for COHb approaching 20%. Such high effect thresholds were attributed to the compensatory effect of the increased brain blood flow that accompanies increased COHb.

As COHb due to acute exposure increases above 25–30%, people begin to lose consciousness and eventually, as COHb reaches 60% and above, death ensues. Exact COHb values depend on individual susceptibilities, the underlying state of health and, to some extent, the activity level of the individuals concerned.

The above data have been considered as evidence that carbon monoxide hypoxia produced the effects. It may not be assumed, however, that non-hypoxic

physiological events do not contribute to the effects, because such non-hypoxic effects might be correlated in time and magnitude with COHb. Evidence exists that non-hypoxic events are responsible for impairments that sometimes develop several days after reduction of COHb due to high-level acute carbon monoxide exposure.

Chronic, low-level exposure

There is a growing consensus that for carbon monoxide, as with ionizing radiation, a NOAEL exists. Effectively, a so-called "safe level" is arbitrarily set at a point at which a level of health effects is deemed acceptable. Thus, the setting of a guideline for indoor carbon monoxide involves other considerations than simply scientific considerations of carbon monoxide's toxicity.

Long-term exposures to lower levels of carbon monoxide have far wider-ranging implications for human health than do acute carbon monoxide exposures. There are many hundreds of millions, indeed billions of people around the world who are currently chronically exposed to carbon monoxide indoors. Such exposure has been reported to alter health in a number of ways, including physical symptoms, sensory–motor changes, cognitive memory deficits, emotional–psychiatric alterations, cardiac events and low birth weight. The evidence for this is derived from clinical toxicological, medical and neuropsychological case reports, case series and other retrospective studies. It is established that many cases of carbon monoxide toxicity are misdiagnosed because the symptoms mimic other health problems.

Epidemiological studies involving large population groups, where exposures are generally at relatively low carbon monoxide levels, have demonstrated increased incidences of low birth weight, congenital defects, infant and adult mortality, cardiovascular admissions, congestive heart failure, stroke, asthma, tuberculosis, pneumonia, etc. In both accidental exposure and epidemiological studies, toxic substances other than carbon monoxide were often present in the exposed person's inhaled air. Dose–effect relationships are suggested in some epidemiological studies. The body of literature from both kinds of study is large and growing, and is consistent with subtle but often profound health effects at low carbon monoxide levels.

Health damage resulting from chronic, lower-level exposure has been difficult to fully explain on the basis of hypoxia, hypoxaemia and measured COHb, since various physiological mechanisms should quickly compensate. This leads to the conjecture that non-hypoxic mechanisms may be responsible for some of the effects. The lack of good dose–effect relationships in the accidental exposure case study reports also suggests alternative mechanisms of causation. The cellular mechanisms described above from recent experimental studies may well be the avenues by which this health damage occurs.

If COHb and hypoxia are not important factors in chronically generated health effects, then an alternative means of referencing severity of exposure must be used. Since COHb level only recognizes initial carbon monoxide uptake, a better measure is arguably to use the product, carbon monoxide concentration × time (i.e. duration of exposure). This parameter more accurately represents the total dose of carbon monoxide received in long-term carbon monoxide exposure, since duration of exposure is explicitly present.

Specially sensitive people

Groups at highest risk from carbon monoxide exposure include the unborn and those adults, elderly or not, with coronary artery disease, congestive heart failure or potential stroke, those at risk of sudden death, etc. There is almost certainly also a group of individuals who are extraordinarily sensitive to carbon monoxide but who have no obvious health or unusual physiological conditions and thus cannot be readily identified. They represent that fraction of individuals who lie at the left end of the standard curve when health effects are determined in any population with known exposure history. All of these higher risk groups must be considered when setting carbon monoxide guidelines for indoor air or, for that matter, outdoor air, i.e. the guideline must be low enough to protect all those at highest risk.

Quality and weight of evidence

Compelling evidence of carbon-monoxide-induced adverse effects on the cardiovascular system is derived from a series of controlled human exposure studies of individuals with cardiovascular disease at COHb levels relevant to ambient conditions. Carbon monoxide exposure caused decreases the time to angina and ST-segment changes with COHb levels on the range of 2 to 6%.

Recent epidemiological studies of chronic environmental exposures are coherent with the results of the controlled human exposure studies. Positive associations between ambient carbon monoxide exposure and ED visits and hospital admissions for ischemic heart disease, congestive heart failure and cardiovascular disease are seen in multiple locations where ambient carbon monoxide concentrations ranged from 0.6 to 10.9 mg/m^3. These carbon monoxide associations generally remained robust in multiple pollutant models. In addition, newer data on pathophysiological mechanisms offer an eventual possible explanation of the chronic effects. These two lines of data support a direct effect of carbon monoxide exposure on cardiovascular morbidity and are considered to have a high weight of evidence.

The toxicological studies of carbon monoxide effects on human birth outcomes and fetal development have been critically reviewed. There is evidence that carbon monoxide exposure during pregnancy is associated with reduced fe-

tal growth and low birth weight. Because of inconsistencies in data reporting, exposure assessment and possible confounding of effects by co-pollutants the weight of this evidence is considered limited but suggestive of important health effects.

At the present time, the strength of the evidence for important health outcomes is as summarized in Table 2.4.

Table 2.4. Strength of evidence

Sufficient evidence of a causal relationship	Acute exposure-related reduction of exercise tolerance and increase in symptoms of ischaemic heart disease (e.g. ST-segment changes)
Sufficient evidence of a relationship	Chronic epidemiological studies of cardiovascular morbidity (heart attack, congestive heart failure , ischaemic heart disease)
	Associations between short-term exposure to carbon monoxide and hospital admissions or emergency department visits for respiratory complaints derived from chronic time-series studies
Limited or suggestive evidence of a relationship	Low birth weight, congenital defects and infant mortality
	Total mortality
	Increased risk of cardiovascular mortality and stroke
	Asthma, bronchiolitis, sinusitis, tuberculosis, pneumonia, etc.
	Neurological, neuropsychological and psychiatric deficits (human and animal studies)
	Effects on the developing auditory system
	Immunological impairment (animal studies)

Guidelines

The 24-hour guideline

Chronic carbon monoxide exposure is different from acute exposure in several important respects, as noted above. Thus, a separate guideline is needed to address minimal exposure over 24 hours, rather than the 8-hour period used in the acute guidelines. The latest studies available to us in 2009, especially those epidemiological studies using very large databases and thus producing extremely high-resolution findings, suggest that the appropriate level for carbon monoxide in order to minimize health effects must be positioned below the 8-hour guideline of 10.5 mg/m^3, possibly as low as 4.6–5.8 mg/m^3. This is also essential since the minimal exposure time for this guideline is three times longer.

Derivation of a concentration–response factor

Exposure to carbon monoxide reduced maximum exercise ability in healthy, young individuals and reduced the time to angina and, in some cases, the time

to ST-segment depression in subjects with cardiovascular disease, albeit at a concentration that was lower than that needed to reduce exercise ability in healthy individuals.

The relationship of carbon monoxide exposure and the COHb concentration in blood can be modelled using the differential Coburn-Forster-Kane equation *(3)*, which provides a good approximation to the COHb concentration at a steady level of inhaled, exogenous carbon monoxide. Based on the laboratory studies of reduction in exercise capacity in both healthy individuals and volunteers with cardiovascular disease, it was determined that COHb levels should not exceed 2%. The CFK equation is used below to determine the levels of carbon monoxide to which a normal adult under resting conditions for various intervals can be exposed without exceeding a COHb level of 2%.

The previous WHO guidelines were established for 15 minutes to protect against short-term peak exposures that might occur from, for example, an unvented stove; for 1 hour to protect against excess exposure from, for example, faulty appliances; and for 8 hours (which is relevant to occupational exposures and has been used as an averaging time for ambient exposures). We do not recommend changing the existing guidelines. However, chronic carbon monoxide exposure appears different from acute exposure in several important respects. Thus, a separate guideline is recommended to address 24-hour exposures. This is also relevant because the epidemiological studies (based on 24-hour exposures) using very large databases and thus producing extremely high-resolution findings are now available and indicate important population-level effects at levels that might be lower than the current 8-hour limit. We recommend a series of guidelines relevant to typical indoor exposures, as shown in Table 2.5.

Table 2.5. Indoor carbon monoxide guidelines

Averaging time	Concentration (mg/m^3)	Comments
15 minutes	100	Excursions to this level should not occur more than once per day Light exercise
1 hour	35	Excursions to this level should not occur more than once per day Light exercise
8 hours	10	Arithmetic mean concentration Light to moderate exercise
24 hours	7	Arithmetic mean concentration Awake and alert but not exercising

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome for guideline definition

Acute exposure-related reduction of exercise tolerance and increase in symptoms of ischaemic heart disease (e.g. ST-segment changes).

Source of exposure–effect evidence

Laboratory dose–effect experiments with human subjects with stable angina exposed to carbon monoxide *(173–178)*. COHb elevated above 2% caused ST-segment changes and decreased time to angina. The CFK equation *(3)* was used to calculate exposure levels to which a normal adult under resting conditions can be exposed for various intervals without exceeding 2% COHb to calculate guideline levels.

Supporting evidence

- Laboratory dose–effect exercise experiments in non-angina (normal) subjects *(167–172)*.
- Numerous epidemiological studies on effects of acute and chronic exposure to carbon monoxide, including studies on health effects when daily mean levels were in the range 0.6–10.9 mg/m^3, provide sufficient evidence of a relationship between long-term exposure and cardiovascular morbidity *(145–157)*.

Results of other reviews

- *Air quality guidelines for Europe*, 2nd ed. *Chapter 5.5, carbon monoxide*. The guidelines were established for 15 minutes (100 mg/m^3), for 1 hour (35 mg/ m^3) and for 8 hours (10 mg/ m^3) *(41,42)*.
- European Commission's INDEX project proposed guidelines: for 1 hour, 30 mg/m^3; for 8 hours, 10 mg/m^3 *(78)*.

Guidelines

15 minutes – 100 mg/m^3.
1 hour – 35 mg/ m^3.
8 hours – 10 mg/ m^3.
24 hours – 7 mg/m^3.

Comments

The addition of a guideline for 24 hours (7 mg/m^3) to the WHO 2000 guidelines *(41)* to address the risk of long-term exposure.

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3. Formaldehyde

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General description

Formaldehyde (molecular formula H_2-C=O; CAS number 50-00-0) is a colourless gas, flammable and highly reactive at room temperature. Formaldehyde can also be obtained commercially as a 30–50% (by weight) aqueous solution, known as formalin.

In ambient air, formaldehyde is quickly photo-oxidized in carbon dioxide. It also reacts very quickly with the hydroxyl radicals to give formic acid. The half-life estimated for these reactions is about one hour depending on the environmental conditions.

The main chemical and physical properties (of the pure substance) are as follows *(1,2)*: molecular mass 30.03 g/mol; relative vapour density 1.03–1.07 (air = 1); melting point –92 °C; and boiling point –19.1 °C. Formaldehyde is soluble in water (around 400 g/l at 20 °C), ethanol and chloroform and miscible with acetone, benzene and diethylether. The octanol/water partition coefficient (log K_{ow}) is 0.35, the vapour pressure is 5.19×10^5 Pa at 25 °C and the Henry's Law constant is 3.41×10^{-2} Pa.m^3/mol at 25 °C.

Formaldehyde is ubiquitously found in the environment, because it is formed primarily by numerous natural sources and anthropogenic activities. In the environment, it is released through biomass combustion (forest and bush fires) or decomposition and through volcanoes, for example. Anthropogenic sources include direct ones such as on-site industrial emissions and fuel combustion from traffic. Other combustion processes (power plants, incineration, etc.) also represent sources of formaldehyde emissions in the atmosphere. However, formaldehyde is also extensively produced industrially worldwide for use in the manufacture of resins, as a disinfectant and fixative, or as a preservative in consumer products.

All these man-made products and uses are the major indirect sources of formaldehyde, in particular indoors. Finally, it should be noted that secondary formation of formaldehyde occurs in air through the oxidation of volatile organic compounds (VOCs) and reactions between ozone (mainly from outdoors) and alkenes (especially terpenes) have been widely described. The contribution of these secondary chemical processes to the ambient and indoor concentrations is still not fully quantified.

Common techniques to measure formaldehyde concentrations include both integrated active and passive methods. Formaldehyde is generally trapped on a sorbent impregnated with 2,4-dinitrophenylhydrazine (2,4-DNPH). Analysis is then conducted in the laboratory by high-performance liquid chromatography and ultraviolet detection at 350 nm. Detection and quantification limits around 1 μg/m^3 can be achieved. The use of an ozone scrubber is recommended to remove the latter from the sample stream to prevent interference during the analysis. Recent comparisons of formaldehyde measurement techniques have shown that, in the presence of low relative humidity, 2,4-DNPH-based methods could underestimate concentrations *(3,4)*.

Conversion factors

At 760 mmHg and 20 °C, 1 ppm = 1.249 mg/m^3 and 1 mg/m^3 = 0.801 ppm; at 25 °C, 1 ppm = 1.228 mg/m^3 and 1 mg/m^3 = 0.814 ppm.

Sources and pathways of exposure

Indoor sources may be combustion processes such as smoking, heating, cooking, or candle or incense burning *(1,5)*. However, major sources in non-smoking environments appear to be building materials and consumer products that emit formaldehyde *(5,6)*. This applies to new materials and products *(7)* but can last several months, particularly in conditions with high relative humidity and high indoor temperatures *(8)*.

Formaldehyde sources in indoor environments include: furniture and wooden products containing formaldehyde-based resins such as particleboard, plywood and medium-density fibreboard; insulating materials (in the early 1980s, urea formaldehyde foam insulation was a major source of indoor pollution); textiles; do-it-yourself products such as paints, wallpapers, glues, adhesives, varnishes and lacquers; household cleaning products such as detergents, disinfectants, softeners, carpet cleaners and shoe products; cosmetics such as liquid soaps, shampoos, nail varnishes and nail hardeners; electronic equipment, including computers and photocopiers; and other consumer items such as insecticides and paper products.

As mentioned above, secondary formation of formaldehyde occurs indoors through chemical reactions between, for example, ozone and terpenes *(9,10)*.

Taking all the indoor sources of formaldehyde into account, it is difficult to identify the major ones that contribute to indoor levels. During a large-scale indoor survey carried out between 1997 and 1999 in 876 homes in the United Kingdom, Raw et al. *(11)* found that, depending on the age of the building, the presence of particleboard flooring in the home was the second most important determinant of indoor concentration. Clarisse et al. *(12)* measured formaldehyde in the bedroom, the kitchen and the living room of 61 Parisian flats with no previous history of complaint for olfactory nuisance. They found that indoor levels

depended on the age of wall or floor coverings (renovations less than one year old), smoking and ambient parameters (carbon dioxide levels and temperature). Using emission factors from the literature, the German Federal Institute for Risk Assessment found that pressed wood products were the major sources contributing to exposure through inhalation at home *(13)*. Marchand et al. *(14)* carried out aldehyde measurements in 162 homes in the Strasbourg area in 2004–2005. Variance analyses showed that formaldehyde concentration was a function of the age of the ceiling coverings for both bedrooms and living rooms. Formaldehyde concentrations tended to decrease with increasing furniture age for both living rooms and bedrooms, but the analyses were not significant. In Canada, Gilbert et al. *(15)* measured formaldehyde levels in 96 homes in Quebec City in 2005. Formaldehyde concentrations were negatively correlated with air exchange rates. They were significantly elevated in homes heated by electricity, in those with new wooden or melamine furniture purchased in the previous 12 months, and in those where painting or varnishing had been done in the sampled room in the previous 12 months. Similarly, relative high levels that can be measured in schools are usually considered to be linked to the high density of furniture in the classrooms (and to poor ventilation).

The possible routes of exposure to formaldehyde are inhalation, ingestion and dermal absorption. Almost no data are available in the literature on dermal exposure *(16)*. Concerning the oral pathway, exposure through food may not be negligible. Estimates of daily formaldehyde intake by six age groups of the general population in Canada were carried out to determine the relative contributions from different media *(17)*. These calculations indicate that daily formaldehyde intake via inhalation is much lower than for intake from food. However, since critical effects associated with exposure to formaldehyde are directly linked to the site of contact, inhalation and ingestion are usually considered separately. Considering exclusively inhalation, indoor exposure contributes up to 98% to the integrated exposure (considering time–activity patterns and daily inhalation volume) *(16)*.

Indoor concentrations and relationship with outdoor levels

A large review of formaldehyde concentrations worldwide in all types of indoor environment, including mobile homes, has been summarized by Salthammer et al. *(5)*. A second large review compiles information on indoor, outdoor and personal exposures to formaldehyde *(18)*.

During a large indoor air survey carried out in homes by the Building Research Establishment (BRE) in the United Kingdom in 1997–1999, the geometric mean, 95th percentile and maximum value of three-day samples of formaldehyde in bedrooms (n = 833) were, respectively, 22.2, 61.2 and 171 $\mu g/m^3$ *(11)*.

During Phase IV of the German longitudinal environmental survey 2003–2006 (GerES IV), formaldehyde was measured through passive samplers for one

week in bedrooms of a randomly selected population of children and teenagers. The geometric mean, 95th percentile and maximum concentration (n = 586) were, respectively, 23.3, 47.7 and 68.9 μg/m^3 *(19)*. These levels were lower than the concentrations measured previously in the framework of the GerES.

In the EXPOLIS study in Helsinki, the average air concentration of formaldehyde in homes was 41.4 μg/m^3 (range 8.1–77.8 μg/m^3) and at the workplace 15 μg/m^3, whereas average personal exposure was 26.8 μg/m^3 *(20)*.

Hutter et al. measured formaldehyde concentrations in 160 Austrian homes and found a median concentration of 25 μg/m^3 and a maximum value of 115 μg/m^3 *(21)*.

The French Observatory on Indoor Air Quality carried out a large monitoring campaign in 567 randomly selected dwellings between 2003 and 2005. The median concentration, 95th percentile and maximum value of formaldehyde following seven days of passive sampling in bedrooms (n = 554) were, respectively, 19.6, 46.7 and 86.3 μg/m^3 *(22)*.

In Canada, Gilbert et al. *(15)* measured formaldehyde levels in 96 homes in Quebec City between January and April 2005. The indoor concentrations ranged from 9.6 to 90 μg/m^3, with a geometric mean of 29.5 mg/m^3.

In the National Human Exposure Assessment Survey (NHEXAS) in Arizona, the median and 90th percentile indoor concentrations were, respectively, 21 and 46 μg/m^3, about the same levels as those measured in Europe *(21)*.

Dingle & Franklin *(23)* observed, in a study carried out in 185 homes in Perth, Australia, indoor formaldehyde concentrations of between 2.5 and 133.7 μg/m^3, i.e. the same range of concentrations as measured in other countries.

Formaldehyde concentrations in Japanese dwellings have been regularly measured within large-scale monitoring campaigns since the 1090s *(24,25)*. The National Institute of Health Sciences conducted a first national field survey in 230 houses in 1996 and found an arithmetic mean concentration of 78 μg/m^3 (range 5–600 μg/m^3). During the last survey conducted in 2005 (n = 1181 homes), the arithmetic mean decreased to 31 μg/m^3 (maximum concentration 300 μg/m^3). In between, the Japanese authorities amended the national building codes and instituted restrictions on the use of formaldehyde-emitting materials for interior finishing.

In China, a large number of monitoring results are available for new homes, since it is mandatory to check whether the maximum allowable formaldehyde concentration in residential buildings (100 μg/m^3) has been exceeded *(26)*. The mean concentration in approximately 6000 recently refurbished dwellings in urban areas was 238 μg/m^3 (remodelled after one year or less; measurements conducted between 1999 and 2006; mean outdoor level around 12 μg/m^3).

Formaldehyde concentrations in dwellings vary according to:

- the age of the building, since the release of formaldehyde decreases with time *(11)*;

- temperature and relative humidity *(8)*;
- the air exchange rate *(11,15)*; and
- the season *(11)*.

Moreover, indoor concentrations can reach more than 200 μg/m^3 close to somebody who is smoking in a room *(27)*. There are many fewer data on offices compared to the residential environment.

A large monitoring campaign carried out in Germany between 2001 and 2004 in 419 rooms found a median indoor formaldehyde concentration of 28 μg/m^3 *(28)*.

Over the period 2004–2007, the EU's Joint Research Centre in Ispra, Italy monitored priority pollutants, including formaldehyde, in European public buildings and environments where children frequently stay, such as schools and kindergartens *(29)*. Formaldehyde concentrations in offices in public buildings (n = 94) varied from 3 to 33 μg/m^3.

Formaldehyde concentrations were measured between 2001 and 2006 in office buildings in southern Finland *(30)*. The occupants had complained of symptoms, but inspection by indoor air experts had not revealed any sources of pollutants. The mean formaldehyde concentration and maximum value were found to be 11 and 44 μg/m^3, respectively.

In the United States, within the framework of the Building Assessment Survey and Evaluation (BASE) study *(31)*, 100 office buildings were investigated between 1994 and 1998. Formaldehyde was detected in all the buildings. The 50th and 95th percentiles were 15 and 32 μg/m^3, respectively.

In China, the mean formaldehyde concentration in 351 offices located all over the country (data from 1996–2005) was of the same order of magnitude as in recently refurbished dwellings, i.e. 256 μg/m^3 *(26)*. In Hong Kong SAR, formaldehyde was measured in 422 air-conditioned offices; the geometric mean was found to be equal to 32 μg/m^3 (± 2.7 μg/m^3) *(32)*.

In France, in the frame of the International Study on Asthma and Allergies in Childhood (ISAAC), formaldehyde was measured in 1999 in 401 classrooms in 108 schools located in 6 cities (Strasbourg, Créteil, Reims, Marseille, Bordeaux and Clermont-Ferrand) *(33)*. Concentrations varied from 4 to 100 μg/m^3 with a mean value of 27 μg/m^3. In 50 Parisian kindergartens studied between 1999 and 2001, both in winter and in summer (n = 222), indoor formaldehyde concentrations ranged from 1.5 to 56 μg/m^3 with a median value of 14 μg/m^3 *(34)*.

In Germany, the indoor air quality was evaluated in 92 classrooms in the winter of 2004/2005 and in 75 classrooms in the summer of 2005 in southern Bavaria. Indoor formaldehyde concentrations ranged from 3.1 to 46.1 μg/m^3 *(35)*.

Formaldehyde concentrations measured in European kindergartens by the EU's Joint Research Centre between 2004 and 2007 (n = 57) varied from 1.5 to 50 μg/m^3, with an arithmetic mean of 17.4 μg/m^3 *(29)*.

In Japan, formaldehyde concentrations measured in 50 schools in 2000 were around 14 μg/m^3 in winter and 30 μg/m^3 in summer *(36)*.

Outdoor air does not contribute to indoor pollution (or the contribution is minor) since ambient levels are generally rather low. Mean ambient air background concentrations remain low compared to those indoors, typically around 1–4 μg/m^3. Data from the HEXPOC report *(16)*, collected from Brazil, Canada, Germany, Italy, Mexico, the Netherlands and the United States, provide ambient concentrations of 1.5–16.4 μg/m^3 with a mean value of 7.2 μg/m^3 (SD = 5.1 μg/m^3). Consequently, the indoor : outdoor ratio is always far above 1. Formaldehyde can be qualified as a very specific indoor pollutant.

Kinetics and metabolism

Absorption

Owing to its solubility in water, formaldehyde is rapidly absorbed in the respiratory and gastrointestinal tracts and metabolized. More than 90% of inhaled formaldehyde gas is absorbed and rapidly metabolized to formate in the upper respiratory tract *(37)*. In rats, it is absorbed in the nasal passages *(38,39)*; in primates, some absorption takes place in the nasal cavity as well as in the nasopharynx, trachea and bronchi *(40,41)*. The mucociliary apparatus is an important defence system in the respiratory tract and may provide protection of the underlying epithelium from gases and vapours *(42)*. Given the solubility of formaldehyde in mucus (water) and estimates of total mucus flow, as much as 22–42% of inhaled formaldehyde may be removed by mucus flow *(37,43)*. It has been shown that when formaldehyde is mixed with particles, more of it is retained by the respiratory tract than when it is inhaled alone. This suggests that some particles can bind with gases and increase the retained dose of a gas *(44)*. However, some estimates show that the deposited dose of formaldehyde in the particle phase is substantially smaller than the dose from the vapour phase *(45)*.

Formaldehyde is absorbed rapidly and almost completely from the rodent intestinal tract *(39,46)*. Although formaldehyde or its metabolites can penetrate human skin – it induces allergic contact dermatitis in humans – dermal absorption appears to be very slight *(47,48)*.

Endogenous sources of formaldehyde

In humans, as in other animals, formaldehyde is an essential metabolic intermediate in all cells. It is produced endogenously from serine, glycine, methionine and choline, and it is generated in the demethylation of N-, O- and S-methyl compounds. It is an essential intermediate in the biosynthesis of purines, thymidine and certain amino acids *(49)*.

Owing to its high reactivity at the site of contact and rapid metabolism, exposure of humans, monkeys or rats to formaldehyde by inhalation does not alter the concentration of formaldehyde in the blood from that endogenously present,

which is about 2–3 mg/l for each of the three species. This concentration represents the total concentration of both free and reversibly bound endogenous formaldehyde in the blood. The absence of an increase is explained by the fact that formaldehyde reacts rapidly at the site of contact and is swiftly metabolized by human erythrocytes, as described below. From a mathematical model describing the absorption and removal of inhaled formaldehyde in the human nose, it was predicted that exposures in the range of 0.125–12.5 mg/m^3 only cause extremely small increases in formaldehyde concentrations compared to the pre-exposure concentrations *(50)*. Intravenous administration of formaldehyde to dogs, cats and monkeys also does not result in accumulation of formaldehyde in the blood, largely owing to its rapid metabolism *(1,39,46)*.

Distribution

Following a 6-hour inhalation exposure of rats to formaldehyde, about 40% of the inhaled compound was eliminated as expired carbon dioxide over a 70-hour period; 17% was excreted in the urine, 5% was eliminated in the faeces and 35–39% remained in the tissues and carcass, indicating that absorbed formaldehyde and its metabolites are rapidly removed by the mucosal blood supply and distributed throughout the body *(39)*. In dogs, orally administered formaldehyde results in a rapid increase in formate levels in the blood. In rats, oral exposure results in about 40% being eliminated as carbon dioxide within 12 hours, 10% being excreted in the urine and 1% being excreted in the faeces *(51)*.

Rodents excreted about 6.6% of the dermally applied dose in the urine over 72 hours, while 21–28% was collected in air traps, likely due to the evaporation of formaldehyde from the skin *(52)*. Approximately 22–28% of the compound or its metabolites remained in the body, including the blood and skin at the site of application. In monkeys, less than 1% of dermally applied dose was excreted or exhaled, in contrast to rodents in which nearly 10% was eliminated by these routes. Coupled with the observation of lower blood levels in monkeys than in rodents, the results suggest that the skin of monkeys may be less permeable to aqueous formaldehyde than that of rodents.

Metabolism and elimination

Formaldehyde reacts rapidly at the site of contact and is swiftly metabolized in humans by erythrocytes, which contain the enzymes formaldehyde dehydrogenase and aldehyde dehydrogenase *(53–56)*. Formaldehyde reacts virtually instantaneously with primary and secondary amines, thiols, hydroxyls and amides to form methylol derivatives. Formaldehyde acts as an electrophile and can react with macromolecules such as DNA, RNA and protein to form reversible adducts or irreversible cross-links *(1)*.

Formate, the metabolic product of formaldehyde, is incorporated in normal metabolic pathways or further oxidized to carbon dioxide. This becomes

important when performing fate and transport studies with radio-labelled formaldehyde, as the label appears in all tissues due to the one-carbon pool. Formaldehyde disappears from the plasma with a half-time of about 1–1½ minutes, most of it being converted to carbon dioxide and exhaled via the lungs. Smaller amounts are excreted in the urine as formate salts and several other metabolites *(47)*.

The primary metabolism system for formaldehyde involves an initial spontaneous reaction with glutathione to form S-hydroxymethylglutathione, followed by reaction facilitated by alcohol dehydrogenase to convert the intermediate to S-formylglutathione *(57,58)*. This intermediate is then further metabolized by S-formylglutathione hydrolase to yield formate and reduced glutathione.

Biomarkers of exposure

To determine whether formate is a useful biomarker for human exposure to formaldehyde, urine was examined in veterinary medical students exposed to low concentrations of formaldehyde *(59)*. Exposed students (formaldehyde air concentration < 0.61 mg/m^3 over a 3-week period) were compared to control subjects. The average baseline level of formate in the urine of 35 unexposed subjects was 12.5 mg/l, but this varied considerably both within and among subjects (range 2.4–28.4 mg/l). No significant changes in concentration were detected. Thus formate in urine does not appear to be a useful biomarker for human exposure, especially at low exposure concentrations.

Inhalation of formaldehyde leads to the formation of DNA–protein cross-links in cells at the site of contact, particularly in the nasal respiratory mucosa of rats and monkeys. The formation of these cross-links is a sublinear function of the formaldehyde concentration in inhaled air from 0.86 to 18.4 mg/m^3, and the yield of DNA–protein cross-links at a given inhaled concentration is approximately an order of magnitude lower in monkeys than in rats. There is no detectable accumulation of DNA–protein cross-links during repeated exposure. Application of a pharmacokinetic model to the data obtained in rats and monkeys indicates that the concentration of DNA–protein cross-links in the human nasal mucosa would be lower than those in rats and monkeys *(1,41,60,61)*. No data are available on DNA–protein cross-links in humans *(1)*. Carraro et al. *(62)* have suggested that an immunological assay that measures the humoral immune response of adducts of formaldehyde and human serum albumin could be used as a biomarker of environmental exposure to formaldehyde, but such a marker has not been developed.

Health effects

Identification of studies

The literature for the cancer part was indentified in PubMed with search terms that included "formaldehyde AND DNA-protein crosslink/crosslinks", "formal-

dehyde AND genotoxic/genotoxicity AND blood AND lymphocyte", "lymphatic AND tissue AND nose AND review", "micronucleus AND test AND review", "formaldehyde AND cancer AND meta-analysis", "formaldehyde AND cancer AND humans", "unit risk AND formaldehyde", "Epstein-Barr AND nasopharyngeal cancer AND review", "Hauptmann M AND nasopharyngeal carcinoma", "Hauptmann M AND silver smithing", "silver smithing AND nasopharyngeal carcinoma", "silver smithing AND cancer", "acid AND nasopharyngeal carcinoma AND review", "nickel AND nasopharyngeal carcinoma", "unit risk AND cancer AND review" and "Zhang L AND formaldehyde". References were also obtained from IARC (*1*), Bosetti et al. (*68*) and the European Commission (*64*). Approximately 200 articles were deemed relevant and read. Of these, more than 120 were evaluated in detail; the relevance of these articles is discussed by Nielsen & Wolkoff *(65)*. However, articles were only included here if they were used directly in the derivation of the WHO indoor air guidelines.

For non-cancer effects, publications from the period 1997–2009 were searched with special emphasis on human effects. Except in special cases, animal and in vitro studies were excluded owing to the huge amount of human data. Formaldehyde was searched in combination with the following terms: allergy, asthma(tics), airway (irritation), bronchoconstriction, children, eye (irritation), inflammation, homes, IgE, (nasal) irritation, kindergartens, lung effects, lung function, offices, odour, schools, sensory irritation, sick-building syndrome, sensitization and trigeminal stimulation.

Eczema was not included except if retrieved in the above-mentioned searches. In addition to databases such as PubMed and Google Scholar, recent comprehensive reviews were considered *(66–68)*, including Gilbert *(69)* and international reports *(1,17,64)*.

Of the 170 papers identified (and listed by Wolkoff & Nielsen *(70)*), 90 were included in the discussion presented below addressing human exposure and epidemiological issues (65 studies), children (11 studies), animal studies (8 studies), cell studies (3 studies) and dust (4 studies).

Respiratory effects of formaldehyde

Nasal retention of formaldehyde in the moist layers covering the nasal mucosa exceeds 90–95%. For example, a maximum of 5% formaldehyde reaches the lower airways in dogs *(71)*. The high retention is also deduced from a mouse bioassay, because only sensory irritation of the upper airways has been observed below 5 mg/m^3 formaldehyde *(72)*. Recent computational fluid dynamic calculations at boundary conditions of fast formaldehyde uptake indicate similar total nasal extraction in adults and children (on average 90%), and thus a limited amount of formaldehyde may traverse the nasal cavity *(73)*.

Human exhaled air contains formaldehyde in concentrations in the order of 0.001–0.01 mg/m^3, with an average value of about 0.005 mg/m^3 *(74–76)*.

Table 3.1. Effects on the airways in humans after acute and short-term exposure to formaldehyde

Study	Formaldehyde concentration (mg/m^3)	Subjects
Falk et al. *(78)*	0.13	8 with nasal congestion [a] 8 without nasal congestion
Lang et al. *(79)*	0.3–0.5 0.6 0.6 0.6	21 healthy [a]
Casset et al. *(80)*	0.1	19 dust mite asthmatics [a]
Wantke et al. *(81)*	0.13–0.41 0.27 (mean)	27 medical students [b]
Ezratty et al. *(82)*	0.5	12 grass pollen asthmatics [a]
Krakowiak et al. *(83)*	0.5	10 healthy 10 asthmatics
Harving et al. *(84)*	0.85	15 asthmatics
Kriebel et al. *(85)*	1.3 (mean)	38 physical therapy students [b]
Airaksinen et al. *(86)*	0.08–1.4	95 patients
Chia et al. *(87)*	0.9/0.6 (personal/mean)	150 medical students [b,c] 189 medical students [d]
Akbar-Khanzadeh & Mlynek *(88)*	1.6–3.1 (breathing zone)	50 medical students [b] 36 physical therapy students
Kim et al. *(89)*	0.2–11.2 3.7 (mean)	167 medical students [b] 67 premedical

[a] Double-blind exposure study.
[b] Field epidemiological study.
[c] First-year students.
[d] Control group, third- and fourth-year students.

Effects after acute and short-term exposure to formaldehyde at indoor levels (non-cancer effects)

The effects include odour (which may cause discomfort), sensory irritation to the eyes and upper airways, lung effects (asthma and allergy) and finally eczema. These effects have been discussed in comprehensive reviews during the last decade *(64,66–69,77)*, including international reports *(1,17)*. Selected key studies from the last decade about exposure–response relationships are listed in Table 3.1. They represent controlled, usually double-blind exposure studies, including both sexes, of which some were tested with both questionnaires and objective methods. In addition, Table 3.1 lists a number of epidemiological studies with lung function testing.

Exposure time (minutes)	Health effects
120	Swelling of nasal mucosa among those suffering from nasal congestion
240	Subjective sensory irritation in eyes Increased eye blink frequency No effects on nasal flow and resistance, peak flow or eye redness No effects on lung function (PEF, FEV_1, MMEF)
30	No effects on lung function (PEF, FEV_1) after mouth pre-exposure of formaldehyde Possible decrease of lung function (PEF, FEV_1) after Der p 1 post-exposure
70 days	No significant decrease in PEF 4 students (one smoker) possibly IgE sensitized No specific formaldehyde IgG antibodies of significance No correlation between IgE and symptoms
60	No effects on lung function (FVC and FEV_1) No effects post-exposure to grass pollen
120	No change in inflammatory mediators after 4 and 24 hours No effects on lung function (FEV_1) No specific formaldehyde IgE antibodies No differences between healthy and asthmatics
90	No effects on airway resistance, lung function (FEV_1) and bronchial activity No delayed reactions
150/week	1–1.5 % decrease of lung function (FEV_1) Effect diminished after 4 weeks
30	No or few effects on lung function Few cases of rhinitis
	No differences in $FEV_1$and FVC among 22 randomly selected male and female subjects after first day and after end of dissection period
60–180	No dose–response relationship between increase in lung function (FVC, FEV_1, FEV_3, FEF) and formaldehyde exposure IgE not associated with formaldehyde exposure

Odour. A large number of odour thresholds have been reported for formaldehyde, varying from 0.05 to 0.5 mg/m^3 *(90)*, some of which are listed in Table 3.2. Two recent studies, carried out under controlled olfactometric conditions, indi-

Table 3.2. Selected odour thresholds for formaldehyde

Study	Odour detection threshold (mg/m^3)	Subjects
Berglund & Nordin *(93)*	0.068	22 non-smoking (women, age-matched)
	0.116	22 smoking (women, age-matched)
Lang et al. *(79)*	0.19–0.36	21 healthy (men and women) [a]
Nagata *(91)*	0.2–0.3	6 adults (expert panellists)

[a] Olfactory perception differs significantly from background.

cate that the odour threshold lies between 0.2 and 0.4 mg/m^3 *(79,91)*; this also agrees with the fact that 33 subjects (mean age 30 years) perceived formaldehyde at about 0.3 mg/m^3 (0.25 ppm) *(92)*. Lower values down to about 0.1 mg/m^3, obtained under conditions of careful generation and monitoring of formaldehyde, have been reported for women *(93)*. Olfactometric determination of odour thresholds depends on a number of experimental factors, such as air purity of the background, and possibly also personal factors such as smoking status and previous olfactory experience; generally, however, it is considered that lower values have higher validity than higher values *(94)*. In addition, recent olfactometric studies indicate less intra- and inter-variability of sensitivity among subjects than in previous studies *(94)*. In view of the above-mentioned studies, it is considered that a significant fraction of the population may perceive formaldehyde at or below 0.1 mg/m^3.

Both eye and upper airway sensory symptoms may be over-reported by odour cues, which cause perceptual uncertainty because of the difficulty of separating the simultaneous and integrated input from odours and sensory irritants *(95,96)*. The perceived odour intensity will depend on a number of psychological factors, such as information about the risk of the chemical *(97)*.

Sensory irritation. Generally, sensory irritation (nasal pungency) is perceived as an unpleasant sensation from the eyes and airways caused by stimulation of the trigeminal nerve endings by airborne sensory irritants *(95)*. A number of reviews have assessed the threshold for self-reported sensory irritation. In general, the eyes are considered to be more sensitive to such irritants than the upper airways *(95)*. Values have been suggested of from 0.15 up to 1.25 mg/m^3 *(66,67,77)*. Raw data on exposure–response relationships obtained from reported human exposure studies about irritating effects were used in a regression model. A value below 0.94 mg/m^3 formaldehyde was considered safe against sensory irritation of the eyes for all workers; about 6% of workers may experience moderate irritation between 0.94 and 1.25 mg/m^3, while none would experience severe irritation *(98)*.

One of the key experimental studies involved 21 healthy subjects exposed double-blind and randomly to formaldehyde for 4 hours *(79)*. Questionnaires and objective methods were used to evaluate eye and airway irritation and lung function. Eye irritation was found to be the most significant effect. Subjective sensory irritation was perceived at as low as 0.38 mg/m^3 for the eyes and 0.63 mg/m^3, with peaks up to 1.25 mg/m^3, for the nose. Adjustment for the personal trait of negative affectivity (e.g. anxiety), however, led to a value of 0.63 mg/m^3 for the eyes at constant exposure and 0.38 mg/m^3 plus four brief peak exposures at 0.63 mg/m^3. An increase in eye blink frequency, which reflects sensory stimulation of the trigeminal nerve but not necessarily in perception thereof, was observed at 0.63 mg/m^3 formaldehyde baseline exposure plus four brief peak exposures at 1.25 mg/m^3, but not without the peak exposures. The nasal flow

resistance and lung function remained unaffected. Eye and nasal irritation did not occur in parallel in the low dose range because eyes are more sensitive; it also to some extent depended on personal factors (e.g. trait and odour). The authors concluded that a corrected lowest observed effect level (LOEL) is 0.63 mg/m^3 without peak exposure, which agrees with the observations of Kulle et al. *(99)*. Lang et al. *(79)* also concluded that the NOAEL for both subjective and objective eye irritation would be close to the LOEL, i.e. 0.63 mg/m^3 at constant exposure; the effects were considered weak, because "less" and "somewhat" were ranked nearly equal. In addition, a slightly lower NOAEL was considered to be 0.38 mg/m^3 with peaks of 0.75 mg/m^3 formaldehyde. Sensory irritation in humans can be predicted from airway responses in mice *(100)*. Further support for the Lang et al. *(79)* estimate is obtained from the mouse bioassay *(72)*, because the NOAEL was found experimentally to be 0.38 mg/m^3.

As a first approximation, the sensory effect of formaldehyde together with other sensory airway irritants is additive *(101)*. However, in a study of 130 women (mean age 27 years) exposed to 0.04 mg/m^3 formaldehyde in a mixture of 23 typical indoor VOCs at a total of 25 mg/m^3 plus ozone (0.08 mg/m^3) for about 140 minutes, neither significant reported sensory irritation nor indication of nasal inflammation was observed *(102,103)*.

No epidemiological study has been identified that unequivocally shows a direct association between formaldehyde and sensory irritation. In general, mixed exposures have encumbered definite conclusions about the effects of formaldehyde *(104–107)* and other explanations have been proposed for the reported symptoms, including psychosocial factors *(108)*. Further, two studies reported no correlation between sensory irritation and formaldehyde concentrations in 23 offices *(30)* and in 59 kitchens *(109)*. Mixed exposures also occur in the wood industry and hamper the interpretation of the effect of formaldehyde. Nasal irritation dominated relative to that of the eyes and throat and was highest among those working with medium-density fibreboard and other wood products. It was concluded that 0.17 mg/m^3 formaldehyde was of minor importance for the reporting of symptoms *(110)*.

The threshold for objective sensory irritation appears to be about 1 mg/m^3 for workers. For the indoor environment (24 hours), a value of 0.125 mg/m^3 was considered safe for the entire population against sensory irritation, including chronic sensory irritation *(66,77)*. This value agrees with results obtained from a recent controlled human exposure study, where no subjective sensory irritation occurred in the eyes and upper airways below 0.38 mg/m^3 formaldehyde *(79)*. Two approaches have been used to protect the potentially more sensitive part of the population. An assessment factor of 4 has been suggested for extrapolation from the NOAEL to a level below the threshold for sensory irritation *(101)*. An assessment factor of 5 has been derived from the standard deviation of nasal pungency thresholds *(111)*. Thus, applying an assessment factor of 5 on the sug-

gested NOAEL of 0.63 mg/m^3 from the studies by Lang et al. *(79)* and Kulle et al. *(99)*, a value of 0.125 mg/m^3 is obtained. This value is also considered valid for children, because there is no indication that children are more susceptible to formaldehyde exposure than adults.

There is no indication that extending exposure beyond four hours would increase the formaldehyde irritative response or the sensitivity. This is based on the fact that the chemical reaction of formaldehyde on the TRPA1 receptor site is reversible *(112,113)*. Inflammation may increase the receptor sensitivity, but neither eye nor airway inflammation has been reported at indoor concentrations of formaldehyde. Further, neither nasal damage nor inflammation was observed in rats during life-long exposure to 1.2 mg/m^3 (1 ppm) formaldehyde *(114)*.

Nasal histopatological changes. A Swedish study *(115)* investigated 70 workers in a chemical plant in which formaldehyde and products based on formaldehyde were produced as resins and, for example, used for impregnation of paper. Additionally, 100 workers employed in the furniture industry were investigated. The 36 controls were mainly clerks. The mean formaldehyde concentration was 0.3 mg/m^3 (range 0.05–0.5 mg/m^3) with frequent formaldehyde peaks above 1 mg/m^3 in the chemical plant. The mean duration of exposure was 10.4 years. The furniture workers were exposed to 0.2–0.3 mg/m^3 formaldehyde that seldom exceeded 0.5 mg/m^3. The mean wood dust concentration was 1–2 mg/m^3 and the mean duration of exposure was 9 years. Controls were exposed to a mean formaldehyde concentration of 0.09 mg/m^3. Nasal biopsies were performed and evaluated by means of a nine-point scale (score 0–8), where category 1 was "stratified cuboid epithelium with loss of ciliated epithelium" and category 2 "mixed stratified cuboid/stratified squamous epithelium".

The mean nasal biopsy score was 1.56 (range 0–4) in the controls, 2.07 (range 0–6) in the furniture workers (not statistically significant) and 2.16 (range 0–4) in the chemical plant (statistically significant). Within the formaldehyde exposure groups themselves, the histopathology scores were not exposure-dependent; exposure metrics were current formaldehyde concentrations (both formaldehyde groups were divided into exposure groups 0.1–0.24, 0.25–0.49 and ≥ 0.5 mg/m^3 formaldehyde), current wood dust concentrations (furniture workers were divided into exposure groups 0.1–1, 1.1–2 and 2.1–4.9 mg/m^3), cumulative formaldehyde exposures (both formaldehyde groups were divided into < 1.5, 1.5–4.99 and ≥ 5 mg/m^3.years) and duration of exposure (< 5, 5–14, 15–24 and ≥ 25 years). Overall, this study cannot be used for risk assessment owing to the lack of an exposure-dependent effect.

Lung effects (non-cancer)

Formaldehyde alone does not cause IgE sensitization *(116,117)*. Recent epidemiological studies of the occupational environment have not indicated an increase

in sensitization to formaldehyde exposure (see below). Nevertheless, formaldehyde-induced sensitization has been hypothesized. Two causes have been suggested, inflammation and formaldehyde acting as an adjuvant for allergens, but they are not supported at normal indoor air concentrations. Inflammatory mediator response was absent on the exposure of human lung epithelial cells at 0.25 mg/m^3 formaldehyde compared to clean air *(118)* and inflammation was not observed in life-long exposure of rats to 1.25 mg/m^3 formaldehyde *(119)*. However, increased lung inflammation, reduced lung function and higher allergen-specific IgE antibody levels have been reported in rodents immunized by intraperitoneal administration to the allergen ovalbumin and followed by different airborne formaldehyde exposures *(116,120,121)*. The interpretation of these studies is not clear in terms of the risk assessment of combined human indoor exposure to formaldehyde and allergens due to intraperitoneal administration in the animals. Thus, evidence of lung effects must depend on human data.

Experimental studies. A number of human exposure studies have been carried out with lung function testing during the last decade (see Table 3.1).

The human exposure studies generally show that lung function is unaffected in both healthy and asthmatic people exposed for 1–4 hours to formaldehyde below 1 mg/m^3 *(79,83,84,88)*. The limited effect on lung function and rhinitis is in agreement with a study in which formaldehyde inhalation had no effect on 95 patients with both upper and lower airway symptoms, when adjusted for placebo effects *(86)*; further, the authors concluded that IgE-mediated formaldehyde allergy was nearly non-existent.

Two studies with asthmatics sensitive to grass pollen and dust mites (Der p 1), respectively, were investigated, in which formaldehyde exposure was combined with post-exposure to the allergens (in a season without grass pollen). In one study, increasing doses of inhaled grass pollen after exposure to 0.5 mg/m^3 formaldehyde for one hour did not affect the lung function over an 8-hour period; a non-significant protective effect of formaldehyde was observed *(82)*. The particle size distribution of the grass pollen was 20–40 μm (V. Ezratty, personal communication, 2010). In the other study, oral breathing of 0.09 mg/m^3 formaldehyde for 30 minutes followed by exposure to dust mites (mean particle size 11 μm) resulted in a bronchial response at a lower dust mite allergen concentration relative to background air with 0.03 mg/m^3 formaldehyde; the geometric mean PD_{20} for Der p 1 was 34 ng after formaldehyde and 45 ng after placebo ($P = 0.05$) *(80)*. An alternative statistical test (Wilcoxon signed-rank test) of the published data showed no significance, thus illustrating how sensitively the statistical outcome depends on the test applied. Further, the effect is considered to have no clinical relevance, because an estimated inhaled allergen dose for 8 hours while resting would be less than 1 ng, based on standard respiratory rates for males, sampled dust mites, e.g. in mattresses *(122)* and assuming a room particle concentration

of 100 μg/m^3. This agrees with measured airborne concentrations of dust mites (Der f 1) in bedrooms *(123)*.

Epidemiological studies (children and adults). Gilbert *(69)* reviewed epidemiological studies on formaldehyde and lung effects in the indoor environment. Studies from the occupational environment have also been evaluated *(1,68)*. Key studies with objective lung function testing are summarized in Table 3.1.

Children. Some case-control and cross-sectional studies have indicated a possible association between low formaldehyde exposure and asthma or sensitization to certain allergens *(106,124–128)*. Briefly, these studies have complex co-exposures, which encumber the establishment of direct cause–effect and dose–response relationships for formaldehyde and the evaluation of confounding effects *(69)*.

Formaldehyde measured in the bedrooms of 224 healthy children aged 6–13 years was not found to be associated with effects on lung function (FEV), but an increase in exhaled nitric oxide was associated with formaldehyde levels greater than 0.06 mg/m^3 *(124)*. Another study was carried out in 80 homes with 148 children aged 7–14 years, of which 53 were asthmatics. An association (OR = 1.40) between formaldehyde exposure and atopy was found with a 0.01-mg/m^3 increase in formaldehyde in the bedrooms. However, no association was identified between formaldehyde in the bedrooms and asthma incidents and lung effects *(125)*. The result is difficult to interpret, because about one third of the children were also exposed to environmental tobacco smoke and possibly pollutants from nearby coal mines and power stations *(129)*. In a third case-control study, formaldehyde was measured twice in homes (bedroom and living room) of 88 asthmatic children under three years of age and a non-asthmatic control group of 104 children *(126)*. A formaldehyde concentration > 0.06 mg/m^3 in the bedroom was found to be associated with an increased risk of asthma. Potential bias could be created by gas heating and new materials in the homes, and the general difficulty of diagnosis in children. Further confounding factors are discussed by Gilbert *(69)*. The most important confounding factor, however, is the presence of combustion products as indicated by reported high concentrations of traffic pollutants such as benzene, toluene, xylenes, nitrogen dioxide and sulfur dioxide in the homes of the children *(130)*. Such pollutants are known to be associated with asthma in children *(131)*, that is, the reported cases may be different apart from asthma and formaldehyde exposure *(132)*. For further information about this particular study and the impact of combustion products and lung effects, see Nielsen et al. *(133)*.

Measured formaldehyde in living rooms and bedrooms did not differ in a univariate analysis between 90 matched pairs of homes of young asthmatics and non-asthmatics aged 4–17 years *(134)*.

The formaldehyde-specific IgE level decreased in 8-year-old children when they moved to a new school with a lower formaldehyde level *(128)*, although no association was identified between formaldehyde and reported symptoms, which encumbers the interpretation. One school study indicated an association between low formaldehyde values and airway effects *(106)*, while another study failed to do so *(135)*. However, the multiple co-exposure of animal allergens, moisture damage (fungi), traffic pollution and socioeconomic factors encumbers interpretation. In addition, chance significance is possible because of the high number of comparisons.

Formaldehyde-specific IgE was measured in 155 Japanese children randomly recruited from outpatient clinics, 122 asthmatics (mean age 9.5 years) and 33 without allergy (mean age 8.8 years) *(136)*. No correlation was found between severity of asthma and IgE levels and formaldehyde, which agrees with the findings of Kim et al. *(137)*. Formaldehyde-specific IgE was detected in only two asthmatic children and only at low levels. One child suffered from severe asthma, while the other had mild asthma.

In a cross-sectional case-control study, comparison of formaldehyde, total volatile organic compounds and dampness in the homes of 193 children (aged 9–11 years) with persistent wheezing and 223 controls showed that formaldehyde may increase wheezing. However, this may be interfered with or dominated by the effects of dampness *(138)*.

In a similar cross-sectional case-control study of children aged 9–11 years, 245 with asthma symptoms within the last year and 329 controls, no association was found between formaldehyde exposure (median concentration 0.037 mg/m^3) in the home and reported asthma, allergy, adverse lung function, bronchial hyperreactivity or sensitization *(139)*.

Adults. Mean exposures of 1.4 ± 0.7 mg/m^3 caused a minor decrease in lung function among students dissecting cadavers *(85)*, an effect that diminished over weeks. Three other studies with exposed students and controls failed to find dose–response relationships *(87–89)*. A limited effect on lung function, and rhinitis, is in accord with a study of 95 patients with both upper and lower airway symptoms related to work that were challenged with inhaled formaldehyde *(86)*. Formaldehyde had no effect when adjusted for placebo effects, and the authors concluded that IgE-mediated formaldehyde allergy was nonexistent.

In a prospective study of 998 pregnant Japanese women, a possible association was identified between formaldehyde levels (median 0.030 mg/m^3, maximum 0.164 mg/m^3) and atopic eczema, but not with asthma, allergy or rhinitis *(140)*. Another prospective study involved 143 Japanese medical students exposed to 3.0 mg/m^3 formaldehyde that responded to a questionnaire before and after a course in anatomy. Two students, one of whom was atopic, showed skin reaction to 1% formaldehyde solution *(141)*. No association was found between reported

asthma in 182 inhabitants from 59 homes and measured formaldehyde levels in their kitchens *(109)*. Eczema, but not allergic respiratory effects, was reported in a study among Finish metal workers exposed to, inter alia, formaldehyde and metalworking fluids *(142)*.

In a cross-sectional study, VOCs and formaldehyde emitted from newly painted surfaces were found to be associated with exacerbated asthma in a study of 252 asthmatics that were compared with 310 non-asthmatics *(127)*. The low number of affected people, multiple exposures (e.g. wood smoke and pets), socioeconomic status and the possibility of chance significance have been suggested as potential sources of bias *(133)*.

In summary, consistent cause–effect and dose–response relationships between formaldehyde and measurable lung effects have not been found in controlled human exposure studies and epidemiological studies below 1 mg/m^3. In general, associations between formaldehyde and lung effects or sensitization in children in homes and schools have not been convincing owing to confounding factors and chance effects *(17,77,132)*.

Release of formaldehyde from wood particles. It has been proposed that particles, such as allergens, may carry formaldehyde down to the lower airways *(132,143)*. Indeed, combined effects between formaldehyde and particles have been reported.

In the only human exposure study, subjects reported more coughing and effects on the lungs when exposed to 0.5 mg/m^3 active charcoal particles (1.4 μm diameter) and 3.5 mg/m^3 formaldehyde *(144)*. These effects are supported by studies on mice and guinea-pigs *(145–147)*, although the results are difficult to interpret for risk assessment because the concentrations are in general orders of magnitude higher than normally found indoors. Further, the amount of releasable formaldehyde from wood particles (> 6 μm) into the respiratory tract has been estimated to be negligible under the conditions in which the particles (5 mg/m^3) were exposed to 0.4 mg/m^3 formaldehyde *(148)*.

The release of formaldehyde from medium-density fibreboard has been measured to lie between 100 and 1000 μg/g dust during 6 hours in water at 35–37 °C *(110,149)*. This shows that the maximum amount of releasable formaldehyde from inhaled dust particles is 2 μg/day for a respirable particle concentration of 100 μg/m^3 and a respiratory rate of 20 m^3/day. Thus, estimated formaldehyde release is insignificant compared to the inhaled amount of gaseous formaldehyde per day (1 mg) at a concentration of 0.05 mg/m^3 *(45,150)* and in agreement with formaldehyde on ambient particles *(151)*.

In summary, the reported studies on formaldehyde in the wood industry indicate that release of formaldehyde into the airways from inhaled particles in indoor environments is negligible compared to the inhalable formaldehyde.

Susceptible groups (non-cancer)

Formaldehyde exposure alone

Paustenbach et al. *(77)*, in their comprehensive review, concluded that hypersensitive groups (elderly people, asthmatics and children) could not be identified, nor could they identify any indication of sensitization by exposure to formaldehyde. This has been supported by comprehensive reviews during the last decade *(66,67)*. Increased sensitivity is not considered biologically plausible. No studies on formaldehyde have been reported that show elderly people to be more susceptible; on the contrary, the elderly are generally less sensitive to sensory irritation *(95)*, possibly decreasing after the age of 60 years *(152,153)*.

Children may breathe more oronasally than adults, in addition to having higher respiration. DNA–protein cross-linking (DPX) has been shown in a computational fluid dynamic nasal model to be about 1.5 higher in adults than in children *(154)*. This suggests that children are not more susceptible than adults, which agrees with predicted formaldehyde adsorption rates per unit surface area of the nasal cavity being equal in children and adults *(73)*.

Combined exposure

One study showed that asthmatics sensitive to grass pollen are insensitive to formaldehyde prior to inhalation of grass pollen *(82)*. Another study indicated that dust mite asthmatics may be more sensitive to a dust mite dose after formaldehyde exposure by mouth *(80)*. The effect is not considered to have clinical relevance. Healthy people that suffer from nasal distress in their homes have been shown to exhibit swelling of the mucosa following exposure to 0.13 mg/m^3 formaldehyde for two hours when compared with a control group *(78)*.

In summary, the experimental and epidemiological literature on formaldehyde does not indicate an increase in susceptibility among children, elderly people and asthmatics. Nevertheless, people with a personal trait of negative affectivity may report more symptoms.

Long-term (carcinogenic) effects of exposure to formaldehyde at indoor levels

Formaldehyde is classified by IARC as carcinogenic to humans (Group 1) *(1)*. In addition to sufficient evidence in experimental animals for upper airway carcinogenicity, IARC concluded that there is sufficient epidemiological evidence that formaldehyde causes nasopharyngeal cancer in humans. This was based on results from the U.S. National Cancer Institute (NCI) cohort and supported by the primarily positive findings in other studies. IARC *(1)* found only limited epidemiological evidence that formaldehyde causes sinonasal cancer in humans and the overall balance of epidemiological evidence did not support a causal role for formaldehyde-induced cancer at other sites, including the oral cavity, oro- and hypopharynx, pancreas, larynx, lung and brain. IARC recently accepted that

there is sufficient evidence that formaldehyde may cause myeloid leukaemia in humans *(155)*. The change in classification of myeloid leukaemia was supported by two new studies *(156,157)*.

Formaldehyde is genotoxic in multiple in vitro models and in exposed humans and laboratory animals *(1,64)*. Studies in humans showed increased DPX in workers exposed to formaldehyde, and genotoxicity and cytotoxicity are considered to play important roles in the carcinogenesis of formaldehyde in nasal tissues *(1)*, where cell proliferation due to cytotoxicity is considered a key element in the development of airway cancer *(64,158)*. For this type of carcinogenic effect, the NOAEL and the use of assessment factors are considered appropriate for setting standards or guidelines for airborne exposures *(159)*. On the contrary, the early risk assessments used linear low-dose extrapolations, which do not account for the sub-linearities in the observed concentration–response relationship *(1)*. The NOAEL approach has been used for setting health-based occupational exposure limits for formaldehyde, for example in Europe *(64)*, Germany *(160)*, Japan *(161)* and the United States *(162)*, and for setting outdoor air standards in Germany *(66)*.

Biological mechanisms

Formaldehyde is a normal component of the blood. In humans, exposure to about 2.5 mg/m^3 airborne formaldehyde did not increase the blood level and exposure to less than 0.6 mg/m^3 did not increase urinary formate excretion owing to rapid metabolism *(1)*. From a mathematical model describing the absorption and removal of inhaled formaldehyde in the human nose, it was predicted that exposures in the range of 0.125–12.5 mg/m^3 cause only extremely small increases in blood formaldehyde levels compared to pre-exposure levels *(50)*. In monkeys, 7.5 mg/m^3 formaldehyde for 6 hours a day, 5 days a week for 4 weeks produced no increase in blood formaldehyde level. In rats, the half-time of formaldehyde is about one minute in the plasma after intravenous administration *(1)*. This indicates that normal indoor air levels of formaldehyde are not expected to increase internal organ exposures.

The mucosal effect in Wistar rats was studied at exposures to 0, 0.125, 1.25 or 12.5 mg/m^3 formaldehyde for 6 hours a day, 5 days a week for 1 year *(163)* and 28 months *(119)*. No histological effect was apparent at 1.25 mg/m^3. In another study, nasal epithelial effects were observed at 2.5 mg/m^3 in Fischer 344 rats exposed for 6 hours a day, 5 days a week for 6–24 months *(164)*. This indicates a NOAEL of 1.25 mg/m^3 for histopathological changes.

In the nasal tissue, formaldehyde reacts with glutathione to form S-(hydroxymethyl)glutathione, which is oxidized by the formaldehyde-dependent alcohol dehydrogenase to produce formate *(1)*. The half saturation of the enzyme is estimated to occur at 3.25 mg/m^3 formaldehyde in the air *(60)* and, thus, higher exposure levels are expected to cause a disproportionate increase in cellular lev-

els of formaldehyde. Formaldehyde causes DPX formation, which is non-linearly related to formaldehyde concentration. A conspicuous increase in DPX formation occurs above 2–4 mg/m^3 *(1)*. In the nasal tissue of animals, DPX is removed rapidly and not accumulated over the exposure period *(1)*.

Nasal cancer in inhalation studies in rats

Chronic exposure to about 7.5 mg/m^3 formaldehyde and above caused squamous cell carcinoma of the nasal cavity of rats *(67,158,165)* with a non-linear concentration–response relationship *(66,158,165)*. Exposure-dependent squamous cell carcinoma has not been observed at 2.5 mg/m^3 (2 ppm) and lower formaldehyde concentrations *(1)*. Further, animal data mostly suggest that organs that are not in direct contact with formaldehyde do not develop neoplasms, presumably due to the fact that formaldehyde is highly reactive and rapidly metabolized locally *(158)*.

The development of squamous cell carcinoma is considered to be related to a genotoxic effect that may be due to DPX *(63,156,164)* in addition to cytolethality-regenerative cellular proliferation *(156,165)*; increased cell proliferation in the rat nose is considered to occur at about 2.5 mg/m^3 formaldehyde and above *(67,158)*.

Lymphohaematopoietic malignancies in animals

Drinking-water studies. Formaldehyde was administered in the drinking-water in a 2-year study in Wistar rats *(168)*. Males were dosed with 0, 1.2, 15 or 82 mg/kg per day and females with 0, 1.8, 21 or 109 mg/kg per day. Each group comprised 50 rats of each sex. Treatment-related pathological effects were limited to changes in the stomach and the kidney in both sexes in the high-dose group; the kidney effect was considered secondary to the reduced intake of liquid. The incidence of tumours did not vary markedly between the groups. Thus, the number of tumour-bearing rats and the total number of tumours were lower in the high-dose males than in the control males.

Haematological tumours were limited to generalized histiocytic sarcoma in one male and myeloid leukaemia in another male, both in the high-dose group. No lymphoma appeared in the high-dose group and no exposure-dependent lymphoma appeared from the study of the auxiliary lymph nodes and the small intestine.

In another study *(169)*, formaldehyde was administered to Wistar rats for up to 24 months at 0, 10, 50 or 300 mg/kg per day. Each group comprised 20 males and 20 females. None of the animals survived 24 months of exposure in the 300-mg/kg group and severe lesions were observed in the stomach. Additionally, serum urea nitrogen increased significantly in both sexes, suggesting an effect on the kidneys. There was no significant difference in the incidence of any kind of tumour among the groups.

In a 104-week study *(170)*, Sprague-Dawley rats were exposed to 10, 50, 100, 500, 1000 or 1500 mg formaldehyde per litre drinking-water. Another group was treated with 15 mg methanol per litre. The treated groups each consisted of 50 males and 50 females, while a control group given tap water consisted of 100 males and 100 females. The animals were observed until they died. There was no difference in survival among the groups, but the number of tumour-bearing animals was significantly higher among males in the highest exposure group. In the female control, methanol and 10, 50, 100, 500, 1000 and 1500 mg/l formaldehyde groups, the percentages of animals with haemolymphoreticular neoplasia were 7, 10, 10, 14, 16, 14, 22[1] and 20[1], respectively. In the males, the percentage was 8, 20, 8, 20, 26[2], 24[1], 22[1] and 46[2], respectively. The study has a number of limitations *(1)*. This applies to the "pooling" of lymphomas and leukaemias ("haemolymphoreticular neoplasia"), the lack of reporting of non-neoplastic lesions, and the absence of information on the incidence of haemolymphoreticular tumours in the historical controls. Further, the incidence in comparison with the methanol-treated group was significantly increased only in the high-dose males, but the dose–response relationship was statistically significant.

Overall, the drinking-water studies showed no consistent increase in lymphohaematopoietic malignancies. Where significant, the effects were at the high formaldehyde levels and exposure–response relationships were apparently non-linear.

Inhalation studies. Groups of approximately 120 male and 120 female Fischer 344 rats and C57BL/6 × $C3HF_1$ mice were exposed to 0, 2.5, 7 or 18 mg/m^3 formaldehyde for 6 hours a day, 5 days a week for 24 months. The exposure period was followed by up to 6 months of non-exposure. Gross pathological examinations were performed on all animals that died or were sacrificed; histopathology was performed on 50 tissue samples per animal in the control and highly exposed groups.

Significantly increased mortality was observed both in male and female rats in the high-dose group and in males in the intermediate group. Survival in female mice was not affected by formaldehyde exposures. Exposed male mice had a slightly poorer survival, but this was not statistically significant. The significant formaldehyde-induced lesions were restricted to the nasal cavity and proximal trachea in both species *(164)*.

The slides from the Kerns et al. *(164)* study were re-evaluated by Woutersen *(114)* as well as by a recent IARC working group (see Baan et al. *(155)* for a list of the working group members) to investigate the occurrence of lymphohaematopoietic malignancies. A mortality-adjusted trend test (the Peto mortality-

[1] $P < 0.05$.
[2] $P < 0.01$.

prevalence test) was used to take into account early deaths due to nasal cancer that might have limited the detection of lymphohaematopoietic malignancies *(114)*. No associations between formaldehyde exposure and leukaemia were seen in male or female rats at the end of the 24-month exposure period or in the 6-month recovery period. In male mice, rare lymphomas were seen at the end of the 24-month exposure period (1%, 1%, 1% and 0%, respectively, in the 0-, 2.5-, 7- and 18-mg/m^3 exposure groups), whereas the trend was highly significant in female mice (17%, 16%, 9% and 29%, respectively). It was concluded that formaldehyde may induce lymphoma in female mice, which is clearly driven by the incidence in the top exposure group.

The IARC working group noted that 12, 17, 16 and 7 out of 120 female rats developed undifferentiated leukaemia in the 0-, 2.5-, 7- and 18-mg/m^3 exposure groups, respectively, and that there was a markedly decreased survival in the 18-mg/m^3 group. Based on a survival-adjusted analysis, the incidence of leukaemia in females exposed to 18 mg/m^3 was increased compared to controls ($P = 0.0056$; Tarone extension of the Cox test, $P < 0.0167$). The working group noted that this is a very common, spontaneously occurring neoplasm in the F344 rat strain.

These re-evaluations permit two conclusions. First, leukaemia may or many not be induced in Fischer 344 rats at 24 months of exposure to 18 mg/m^3, at which a high incidence of nasal tumours occurred. Second, if lymphoma is induced by formaldehyde in female mice, the occurrence is at the very high exposure level at which there was high incidence of nasal tumours in rats. Thus, in rats the occurrence of nasal tumours is a more sensitive end-point than lymphohaematopoietic malignancies.

In another study, 100 Sprague-Dawley rats were exposed to 18 mg/m^3 formaldehyde for 6 hours a day, 5 days a week for life. Complete necropsy was performed on each animal. Histological sections were performed from each lobe of the lung, trachea, larynx, liver, kidney, testes and other organs where gross pathology was present. There was an increased mortality in the formaldehyde group compared with the control group. In the formaldehyde group, three malignant lymphomas were observed. In the similar control group of 99 rats, two malignant lymphomas were observed, while three were observed in 99 colony controls *(171)*.

In a 28-month study, male F-344 rats in groups of 32 were exposed to formaldehyde for 6 hours a day, 5 days a week at 0, 0.38, 2.5 or 18.8 mg/m^3, plus a room control group. The number of rats alive at 18 months or later and thus available for histopathology was 19, 22, 17, 7 and 16, respectively. Haematological, biochemical and pathological examinations were performed. Tissues for histopathology were pituitary, thyroid, nasal region, trachea, oesophagus, stomach, small and large intestine, prostate gland, urinary bladder, muscle, femur, sciatic nerve, spinal cord, mesenteric lymph nodes and any other gross lesion. Increased

mortality was observed at the highest exposure concentration. No microscopic lesions were attributed to formaldehyde exposure except those in the nasal cavity. Also, there was no exposure-related abnormal haematological finding *(172)*.

Overall, the occurrence of lymphohaematopoietic malignancies in inhalation studies in rats and mice is not convincing. In general, there is lack of consistency across species *(165,173)*. Nevertheless, if it is assumed that there is a causal association, the association was seen at high exposure levels, which caused a high incidence of nasal cancer in rats. Also, the exposure–response relationship seems to be non-linear.

Assessment of cancer hazards in meta-analyses

Oral cavity and pharynx, sinus and nasal cavity, and lung. Bosetti et al. *(63)* conducted a meta-analysis based on six cohorts of industrial workers and professionals (pathologists, anatomists, embalmers and undertakers). No significant excess cancer risk was found in industrial workers and professionals for all cancers or for oral and pharyngeal cancer. The lung cancer risk was not affected in industrial workers (RR 1.06; 95% CI 0.92–1.23), whereas the risk was reduced in the professionals (RR 0.63; 95% CI 0.47–0.84). The study concluded that there was no appreciable risk for cancer of the oral cavity and pharynx, sinus and nasal cavity and lung. IARC *(1)* also concluded that the overall balance of epidemiological evidence did not support a causal role for formaldehyde in cancer in the oral cavity, oro- and hypopharynx and lungs.

In the meta-analysis by Bosetti et al. *(63)*, the nasopharyngeal cancer risk was increased in industrial workers, but this was not statistically significant (RR 1.33; 95% CI 0.69–2.56). This was based on eight cancers in one study where six cancers were in one of ten plants and one cancer was from another cohort. No excess brain cancer risk was apparent in the industrial workers (RR 0.92; 95% CI 0.75–1.13) but the risk was significantly increased in the professionals (RR 1.56; 95% CI 1.24–1.96). The brain cancer risk is not consistent across the two types of study and it is not biologically plausible that formaldehyde causes brain cancer. This is in agreement with the evaluation of IARC *(1)*.

Pancreatic cancer was addressed in a meta-analysis that comprised 14 epidemiological studies. No exposure-dependent effect was apparent *(174)*. This is in agreement with the IARC evaluation *(1)*.

Leukaemia was studied in a meta-analysis comprising 18 epidemiological studies *(175)*. Heterogeneity was observed across studies and differences appeared between the RR of formaldehyde exposures in American (RR 1.2; 95% CI 1.0–1.4) and European workers (RR 0.9; 95% CI 0.7–1.1). Furthermore, the RR was different for various types of job: industrial workers (RR 0.9; 95% CI 0.8–1.0), embalmers (RR 1.6; 95% CI 1.2–2.0) and pathologists and anatomists (RR 1.4; 95% CI 1.0–1.9). Only three of the studies *(176–178)* evaluated leukaemia rates by exposure level. This meta-analysis concluded that the data do not pro-

vide consistent support for a relationship between formaldehyde exposure and leukaemia.

In the meta-analysis by Bosetti et al. *(63)*, significantly reduced risks of lymphatic and haematopoietic cancer were observed in the industrial workers (RR 0.85; 95% CI 0.74–0.96). In contrast, the risk was significantly increased in the professionals (RR 1.31; 95% CI 1.16–1.48), comprising pathologists, anatomists and embalmers. No excess in leukaemia risk appeared in industrial workers (RR 0.90; 95% CI 0.75–1.07) but the risk was significantly increased in the professionals (RR 1.39; 95% CI 1.15–1.68).

The most recent meta-analysis that includes all relevant cohort and case-control studies published through May 2009 found no increase in leukaemia. The meta-analysis summary RR was 1.05 (95% CI 0.93–1.20) for cohort studies and the summary OR was 0.99 (95% CI 0.71–1.37) for case-control studies *(179)*.

While the three meta-analyses discussed above reported on the contrast between ever- vs never-exposed subjects and various combinations of lymphohaematopoietic cancers, a recent meta-analysis evaluated especially myeloid leukaemia from the highest exposure group of each study *(180)*. Where several RRs were reported in a study, one RR was selected from each study in the order: peak exposure, average exposure intensity, cumulative exposure, exposure duration. For example, the accepted study groups were exposed to more than 2 ppm on average, with peak exposures above 4 ppm, or were exposed for more than 10 years. In the analysis by Zhang et al. *(180)*, the fixed effects model and the random effect model showed similar results, and therefore the results are from the fixed effects model. Thus, an increased risk was observed for all types of cancer combined (RR 1.25; 95% CI 1.12–1.39; N = 19), for all leukaemia (RR 1.54; 95% CI 1.24–1.91; N = 15), for myeloid leukaemia (RR 1.90; 95% CI 1.41–2.55; N = 6) and for multiple myeloma (RR 1.31; 95% CI 1.02–1.67; N = 9) but not for Hodgkin's lymphoma (RR 1.23; 95% CI 0.67–2.29; N = 8) or non-Hodgkin's lymphoma (RR 1.08; 95% CI 0.86–1.35; N = 11).

The increases in leukaemia, myeloid leukaemia and multiple myeloma in the Zhang et al. *(180)* study were not consistently observed in the other studies *(63,175)*. This may be explained by the fact that, if these types of cancer are caused by formaldehyde, they appear at high levels of formaldehyde.

Cancer hazard studies in occupational cohorts

To obtain concentration–response relationships for formaldehyde exposures based on human experiences, the cancer risk due to formaldehyde exposure is reviewed from the three largest and recently updated occupational cohorts, which were identified from IARC *(1)*, from the formaldehyde documentation for setting a health-based occupational exposure limit by the Scientific Committee on Occupational Exposure Limits *(64)* and a recent review *(63)*. The NCI cohort comprised 25 619 workers employed in 10 facilities producing or using for-

Table 3.3. Cancer risks from formaldehyde exposure[a]

Cancer	Study[b]											
	NCI cohort *(175,179)*[c]			NCI cohort *(180)*			British cohort *(174)*[d]			USA garment worker cohort *(176)*[e]		
	ICD-8[f]	O/E	SMR	ICD-8[f]	O/E	SMR	ICD-9[f]	O/E	SMR	ICD-9[f]	O/E	SMR
All cancers	140–209	1916[g]/–[h]	0.90*	–	–	1.07*	140–208	1511/1375.2	1.10*	140–208	608/–	0.89*
Nose and nasal sinuses	160	3/–	1.19	–	–	–	160	2/2.3	0.87	160	0/0.16	–
Pharynx				–	–	–	146–149.1	15/9.7	1.55	146–149	3/–	0.64
Nasopharynx	147	8[i]/–	2.10*				147	1/2	–	147	0/0.96	–
Larynx	161	23/–	0.95	–	–	–	161	14/13.1	1.07	161	3/–	0.88
Lung	162	641/–	0.97	–	–	–	162	594/486.8	1.22*	162	147/–	0.98
Bone	170	7/–	1.57				170	6/3.5	1.73	–		
Prostate	185	131/–	0.90	–	–	–	185	80/99.4	0.80	185	11/–	1.58
Hodgkin's lymphoma	201	20/–	1.26	201	25/–	1.42	201	6/8.5	0.70	201	2/–	0.55
Non-Hodgkin's lymphoma	200	44/–	0.61*	200	94/–	0.85	200	31/31.7	0.98	200	5/–	0.85
	202			202			202.0					
							202.1					
							202.8					
Multiple myelomas	203	28/–	0.88	203	48/–	0.94	203.0	15/17.5	0.86	–		
Leukaemia	204–207	65/–	0.85	204–	116/–	1.02	204–208	31/34.1	0.91	204–208	24/–	1.09
Lymphatic leukaemia				207	36/–	1.15						
Myeloid leukaemia	205	–/–	–	204	44/–	0.90			0.89[j]	205	15/–	1.44
Stomach	–			205	–	–	151	150/114.4	1.31*	151	13/–	0.80
All digestive	150–159	420/–	0.89*	–			–		–	150–159	16/–	0.77*

[a] Standardized mortality ratio (SMR), observed cases (O), expected cases (E) and the ratio (O/E). When the 95% CI does not include 1.00, it is marked with an asterisk (*).

[b] Comparison with national death rates.

[c] Median average intensity 0.45 and range 0.01–4.25. Exposure to ≥ 2 occurred in 4.7% and 22.6% had peak exposures at ≥ 4.

[d] Range 0.1 to > 2.

[e] Geometric mean 0.15 and geometric standard deviation 1.90. Range 0.09–0.2. Past exposures may have been substantially higher.

[f] International Classification of Diseases, 8th revision (ICD-8) and 9th revision (ICD-9).

[g] In the Hauptmann et al. 2003 study *(177)*, the number of formaldehyde workers who had died was 1916 (2-year lag interval), while in the Hauptmann et al. 2004 study *(181)*, the number was 1723 (15-year lag interval). The lag interval was 2 years in the Freeman et al. study *(182)*.

[h] – = not indicated.

[i] Hauptmann et al. *(181)* (Table 2) report eight nasopharyngeal cancers among formaldehyde-exposed workers that were used for the SMR calculation. Although one subject was misclassified on the death certificate, this subject was retained in the SMR calculation since population reference rates are based on death certificates. Also, the exact 95% CI was reported to be 0.91–4.14 and thus the SMR value of 2.10 is not statistically significant. The seven cases in the text and in Tables 3–6 of Hauptmann et al. *(181)* were used for calculation of relative risks.

[j] Estimated by Cole & Axten *(183)* for the highly exposed group (> 2 ppm).

maldehyde. Workers were employed prior to 1 January 1966 and were followed through to 31 December 1994 *(177,181)* and recently through to 31 December 2004 for lymphohaematopoietic malignancies *(182)*. A cohort from six British factories, comprising 14 014 men employed after 1937, was followed through to December 2000 *(176)*. The U.S. National Institute for Occupational Safety and Health (NIOSH) established a cohort of 11 039 employees in three garment facilities; the study was updated through to 31 December 1998 *(178)*.

The cancer risks obtained from the three studies are shown in Table 3.3. The table is limited to anatomical sites that are directly exposed to airborne formaldehyde and to other sites where excess risks have been reported.

Nasopharyngeal cancer

The relative risk of nasopharyngeal cancer was further evaluated by four metrics: average exposure intensity (mg/m^3), highest peak exposure (mg/m^3), cumulative exposure (mg/m^3-years) and duration of exposure (years). In the average exposure intensity metric and the highest peak exposure metric, RRs were obtained with the unexposed group as the reference group. In the three average intensity exposure groups, > 0 to < 0.63 mg/m^3, 0.63 to < 1.25 mg/m^3 and ≥ 1.25 mg/m^3, the respective RRs were: not obtainable (0/3640 deaths), 0.38 (1/1405 deaths) and 1.67 (6/1450 deaths). Apparently, the increased risk was due to exposures ≥ 1.25 mg/m^3, although the trend was not statistically significant. With the peak exposure metric, all exposed deaths were in the highest peak exposure group (≥ 5 mg/m^3) and the trend was statistically significant. An exposure-dependent trend was found for the cumulative exposure metric *(181)*, which was apparently driven by the highest exposure level.

Later, it was shown that the excess occurrence of nasopharyngeal cancer in the NCI study was driven by one of the 10 plants studied, where 6 of the 10 cases occurred. In this plant, the cases might or might not have been caused by formaldehyde exposure but by other risk factors such as "silver smithing" and "silver smithing or other metal work" *(184)*. The only established occupational risk factor, wood dust, was considered a priori, but dropped because of very small numbers *(184)*. Additionally, a low number of nasopharyngeal cancers in the reference group can cause unstable RR estimates *(185)*. However, a recent IARC working group noted that it was unlikely that confounding or bias could explain the observed association *(186)*.

It can be considered, however, for the purposes of indoor air guideline setting, that no excess nasopharyngeal cancer was reported at a mean formaldehyde exposure level at or below 1.25 mg/m^3 and with peak exposures below 5 mg/m^3.

Lymphohaematopoietic malignancies

The NCI study also evaluated the effect of average intensity and peak exposures on the occurrence of lymphohaematopoietic malignancies leading to 178 deaths

(177). The lowest exposure groups were used as reference for evaluation of RRs. For the average exposure intensity, the reference group comprised exposures of 0.125–0.5 mg/m^3.

The two higher exposure groups comprised exposures of 0.6–1.1 and ≥ 1.25 mg/m^3. Lymphohaematopoietic malignancies were significantly increased in both groups, with a borderline significant trend. Hodgkin's lymphoma was significantly increased in the 0.6–1.1-mg/m^3 group, with a significant exposure-dependent trend. Myeloid leukaemia was significantly increased at the highest exposure level, but the trend was not significant. For the peak exposure, the exposure in the reference group was 0.125–2.4 mg/m^3 and the exposure in the two higher exposure groups was 2.5–4.9 and 5 mg/m^3, respectively. Significantly increased RRs were observed for lymphohaematopoietic malignancies and leukaemia in the two highest exposure groups.

In the highest exposure group, the RR for myeloid leukaemia was also increased. For these three diseases, the trend in exposure-dependent effect was statistically significant. Additionally, the exposure-dependent trend was statistically significant for Hodgkin's lymphoma. The RR for leukaemia was not significantly associated with cumulative exposure.

When the study by Hauptmann et al. *(177)* was reanalysed by Marsh & Youk *(187)*, it was shown that excess leukaemia and myeloid leukaemia were strongly influenced by a lower death rate in the reference groups compared to the national and local county SMRs. Using the national and local ratios, the SMRs for all leukaemia and myeloid leukaemia were very close to unity and were not significantly increased in the highest peak exposure category (≥ 5 mg/m^3). To evaluate the robustness of the categorizations, new average exposure intensity categories were constructed whereby the highest exposure category was ≥ 0.93 mg/m^3. Again, using the national and local county rates showed that the SMRs for all leukaemia and myeloid leukaemia were very close to unity and not significantly increased. Also, in this case, cumulative formaldehyde exposures were not associated with the development of leukaemia or myeloid leukaemia. Although this reanalysis does not support a causal association between formaldehyde exposure and leukaemia and myeloid leukaemia, for indoor air guideline setting one can take into account the fact that no excess lymphohaematopoietic malignancies occurred at a mean exposure level of formaldehyde below 0.93 mg/m^3 and where peak exposures were below 5 mg/m^3.

Recently, the NCI study updated lymphohaematopoietic risks through to 31 December 2004 *(182)*. SMRs were estimated from the United States mortality rate (Table 3.3). For lymphohaematopoietic malignancies, the 319 deaths resulted in similar SMRs in exposed and unexposed people: 0.94 (95% CI 0.84–1.06) and 0.86 (95% CI 0.61–1.21), respectively. Exposure-dependent trends were evaluated from exposure categories similar to the previous follow-up. For lymphohaematopoietic malignancies in the average formaldehyde intensity metric, neither

of the two highest exposure groups showed an increased RR, nor was the exposure trend statistically significant. In the new follow-up, the RR for Hodgkin's lymphoma was significantly increased in the 0.63- to < 1.25-mg/m^3 group but not in the highest exposure group (≥ 1.25 mg/m^3). The trend was statistically significant. Similar results appeared in the previous follow-up. Multiple myeloma was significantly increased among the non-exposed but not in the exposed groups. In the previous follow-up, the increase was not significant. In the peak exposure metric, lymphohaematopoietic malignancies were increased significantly in the highest exposure group (≥ 5 mg/m^3) and the trend was significant. Apparently, it is driven by the highest exposure group. Thus, the RR in the next highest exposure group was not remarkably increased (1.17 (95% CI 0.86–1.59)) and close to the RR among the unexposed, which was 1.07 (95% CI 0.7–1.62). In the previous follow-up, the RRs in the two highest exposure groups were similar (1.71 and 1.87, respectively) and significantly increased in both groups. The trend was also significant. In the new follow-up, the RR of Hodgkin's lymphoma was increased significantly in the two highest exposure groups: 3.30 (95% CI 1.04–10.50) in the 2.5- to < 5.0-mg/m^3 group and 3.96 (95% CI 1.31–12.02) in the ≥ 5-mg/m^3 group) with an exposure-dependent trend. In the previous follow-up, the trend was increased significantly but the RRs were approximately of the same size as in the recent follow-up. Except for a statistically increased RR of multiple myeloma in the non-exposed, no other remarkable RR appeared in the peak exposure group in the new follow-up study. For example, the RRs for multiple myeloma were 2.74 (95% CI 1.18–6.37) among the non-exposed, 1.0 in the reference group (≥ 0.13 to < 2.5 mg/m^3), 1.65 (95% CI 0.79–3.61) in the 2.5- to < 5.0-mg/m^3 group and 2.04 (95% CI 1.01–4.12) in the highest peak exposure group (≥ 5 mg/m^3) with no exposure-dependent trend. In this case, the RRs in the exposed groups were lower than in the non-exposed group, which does not support a formaldehyde-dependent effect. In the similar peak exposure groups, the RRs of myeloid leukaemia were 0.82 (95% CI 0.25–2.67), 1.0, 1.30 (95% CI 0.58–2.92) and 1.78 (95% CI 0.87–3.64) with a non-significant trend. In the earlier follow-up, myeloid leukaemia was significantly increased in the highest exposure group (3.46 (95% CI 1.27–9.43)) with a highly significant trend ($P \leq 0.009$).

Summarizing the NCI study, it is of note that the RRs for Hodgkin's lymphoma increase abruptly from that in the reference group (peak exposure > 0 to < 2.5 mg/m^3 and average intensity > 0 to < 0.63 mg/m^3). Overall, as the RRs in the reference group and the non-exposed group were not significantly different, an exposure guideline for formaldehyde should consider that peak exposures should be below 2.5 mg/m^3 and average exposures below 0.63 mg/m^3 to protect against lymphohaematopoietic malignancies in general.

The United Kingdom cohort from six British factories comprised 14 014 men employed after 1937 and followed through to December 2000 *(176)*. By the end of the follow-up, 5185 of the men had died. The overall mortality from all can-

cers was slightly higher than expected from national death rates (SMR 1.10; 95% CI 1.04–1.16), as was that from lung cancer (SMR 1.22; 95% CI 1.12–1.32) and from stomach cancer (SMR 1.31; 95% CI 1.11–1.54) (see Table 3.3). Lung and stomach cancers were further analysed using the local geographical variations in mortality. Lung cancer increased significantly (SMR 1.28; 95% CI 1.13–1.44) only in the highest exposed group where the formaldehyde level was greater than 2.5 mg/m^3. No trend was seen at lower levels and, for example, the SMR in the range 0.75–2.5 mg/m^3 was 0.99 (95% CI 0.74–1.30). However, there was a statistically non-significant decrease in the risk of death from lung cancer with duration of high exposure. The risk showed no increasing trend with time since first exposure. The authors interpreted lung cancer in the highest exposed group to be "rather large to be explained simply by a confounding effect of smoking" (which was not taken into account). Using the local mortality rate, stomach cancer was not exposure-dependent and was considered by the authors to be a less plausible outcome. For setting an indoor air guideline, the key information from this study is that no increase in lung cancer was apparent at formaldehyde levels of 5 mg/m^3 or lower. No results on peak exposures and risk for myeloid leukaemia were provided.

NIOSH established a cohort of 11 039 employees in three garment facilities (The USA garment worker cohort). The study was updated through to 31 December 1998, by which time 2206 of the employees had died. The mortality from all malignant neoplasms was significantly less than expected (SMR 0.89; 95% CI 0.82–0.97), as was that for all digestive neoplasms (SMR 0.77; 95% CI 0.63–0.92). Myeloid leukaemia (ICD-9: 205) was significantly increased (13 deaths; SMR 1.91) after 20 or more years since first exposure, but the trend was not significant. Among workers with both 10 or more years of exposure and 20 years or more since first exposure, multiple-cause mortality from leukaemia was significantly increased almost two-fold (15 deaths; SMR 1.92; 95% CI 1.08–3.17). In addition to underlying cause of death, all causes listed on the death certificate were analysed using multiple cause mortality. Multiple cause mortality from myeloid leukaemia was significantly increased among this group (8 deaths; SMR 2.55; 95% CI 1.10–5.03) *(178)*.

Recent studies on lymphohaematopoietic effects

Haematopoietic tissue damage was studied in 43 formaldehyde-exposed workers and 51 controls. The 8-hour time-weighted average was 1.6 and 0.03 mg/m^3 and the 90 percentile 3.14 and 0.03 mg/m^3, respectively. Peak exposure concentrations were not reported. Formaldehyde exposures were associated with reduced blood lymphocyte, granulocyte, platelet, red blood cell and total white blood cell counts; the total white blood cell count was reduced by 13.5% in the formaldehyde-exposed workers. Urinary benzene concentrations were low in both groups, thus excluding benzene exposure as a confounder. The findings

were considered consistent with a bone-marrow-toxic effect due to formaldehyde. Peripheral blood cells from formaldehyde-exposed and control workers were cultivated to derive blood myeloid progenitor cells. The colony formation fell non-significantly by 20% in the formaldehyde-exposed workers and this was considered a toxic effect on the myeloid progenitor cells. Blood mononuclear cells from volunteers were cultivated in vitro to derive different lines of progenitor cells.

The addition of different dilutions of formalin to the cultures showed that formaldehyde reduced the number of generated colonies from all progenitor cell lines. This showed that formaldehyde can inhibit the proliferation of all progenitor cells if the endogenous formaldehyde level is increased due to formaldehyde exposure. Blood progenitor cells of the myeloid line were derived from 10 highly exposed workers (8-hour time-weighted median concentration 2.67 mg/m^3 and 90th percentile 5.18 mg/m^3) and 12 controls (8-hour time-weighted median concentration 0.03 mg/m^3 and 90th percentile 0.03 mg/m^3). Formaldehyde-exposed workers showed increased monosomy (loss) of chromosome 7 and an increase in trisomy of chromosome 8; these cytogenic changes are observed in myeloid leukaemia and myelodysplastic syndromes *(154)*.

It should be noted that the study has limitations in relation to risk assessment of formaldehyde exposure at indoor air concentrations. First, the exposures are extremely high and thus the unreported peak exposure concentrations may have been at extremes. Second, no exposure–response relationship is established. Third, the very high exposure concentrations may be expected to cause mucosal damage that may influence both the nasal metabolism and absorption into the blood compartment; no information is available on the mucosal tissue. Fourth, the in vitro cell culture study is relevant for mechanistic considerations only, because no increase in formaldehyde has been observed in the blood compartment of humans due to formaldehyde exposure. This is supported by model calculations at about 2.5 mg/m^3 *(50)*. Similar results were reached for extrapolations up to 12.5 mg/m^3, but such extrapolations may be invalidated by the toxic effects on the mucosal membrane above 2.5 mg/m^3. Overall, the interpretation of this study in relation to risk assessment is unclear. For the sake of transparency, it would have been desirable that all measured exposures other than to formaldehyde had been reported.

In a case-control study in the United States *(157)*, 168 professionals employed in the funeral industry who died from lymphohaematopoietic malignancies were compared with 265 deceased matched controls from the same industry. The 8-hour time-weighted average formaldehyde intensity was about 0.125–2.5 mg/m^3, the average intensity while embalming was about 1.9–2.25 mg/m^3 and peak exposure was about 10–13 mg/m^3. Four people died from nasopharyngeal cancer, but only two had been involved in embalming (OR 0.1 (95% CI 0.01–1.2)). No increase was observed in lymphoid malignancies (ICD-8 200–204), in-

cluding Hodgkin's lymphoma (OR 0.5 (95% CI 0.1–2.6)), which was consistently elevated in the previous industrial cohort studies *(177,182)*. The study observed a specific association between embalming and myeloid leukaemia (ICD-8 205). Thus, using a reference group of newer exposed with one case subject, the OR was 11.2 (95% CI 1.3–95.6).

The first analysis of myeloid leukaemia used a reference group of subjects that had not performed embalming. The duration of working in jobs that involved embalming showed a significant trend ($P = 0.02$): in the categories > 0–20, > 20–34 and > 34 years, the OR was 5.0 (95% CI 0.5–51.6), 12.9 (95% CI 1.4–117.1) and 13.6 (95% CI 1.6–119.7), respectively. No significant trend was observed with the number of embalmings. However, several significant ORs were observed. Thus, the number of performed embalmings were divided into > 0–1422, > 1422–3068 and > 3068, where the OR was 7.6 (95% CI 0.8–73.5), 12.7 (95% CI 1.4–116.7) and 12.7 (95% CI 1.4–112.8), respectively. Exposure–response relationships for the different formaldehyde metrics were established. The peak exposure metric was the only metric that showed a significant trend ($P = 0.036$). Peak formaldehyde exposures were divided into > 0–8.75 mg/m^3, > 8.75–11.6 mg/m^3 and > 11.6 mg/m^3, where the OR was 15.2 (95% CI 1.6–141.6), 8.0 (95% CI 0.9–74.0) and 13.0 (95% CI 1.4–116.9), respectively. The cumulative formaldehyde exposures (mg/m^3-hours) were divided into > 0–5073, > 5073–11 566 and > 11 566, where the OR was 10.2 (95% CI 1.1–95.6), 9.4 (95% CI 1.0–85.7) and 13.2 (95% CI 1.5–115.4), respectively. The average formaldehyde intensity while embalming was > 0–1.75 mg/m^3, > 1.75–2.38 mg/m^3 and > 2.38 mg/m^3, where the OR was 11.1 (95% CI 1.2–106.3), 14.8 (95% CI 1.6–136.9) and 9.5 (95% CI 1.1–86.0), respectively. The 8-hour time-weighted formaldehyde intensity was divided into > 0–0.125 mg/m^3, > 0.125–0.225 mg/m^3 and > 0.225 mg/m^3, where the OR was 8.4 (95% CI 0.8–79.3), 13.6 (95% CI 1.5–125.8) and 12.0 (95% CI 1.3–107.4), respectively. The cumulative formaldehyde exposure, the average formaldehyde intensity while embalming and the 8-hour time-weighted average intensity showed no statistically significant formaldehyde exposure-dependent trend. It is noted that, within each of the formaldehyde exposure metrics, the ORs showed little difference and had highly overlapping confidence intervals. This suggests that the statistical significances are driven mainly by exposure vs non-exposure and less by differences in exposure levels. Also, in each of the formaldehyde metrics, none of the trend tests within the formaldehyde groups themselves was statistically significant.

Because of the small number of exposed cases and related instability of the reference group, the authors performed additional exposure–response analyses with a larger reference group, including subjects with low exposure. The second analysis of myeloid leukaemia used a reference group whose members had performed fewer than 500 lifetime embalmings, allowing 5 case subjects in the reference group.

The duration of working in jobs with embalming showed a significant trend ($P = 0.02$). In the categories < 20, > 20–34 and > 34 years, the OR was 0.5 (95% CI 0.1–2.9), 3.2 (95% CI 1.0–10.1) and 3.9 (95% CI 1.2–12.5), respectively. No significant trend was observed with the number of embalmings, but significant ORs were observed at the highest exposure level. Thus, the numbers of performed embalmings were divided into ≥ 500–1422, > 1422–3068 and > 3068, where the OR was 1.2 (95% CI 0.3–5.5), 2.9 (95% CI 0.9–9.1) and 3.0 (95% CI 1.0–9.2), respectively.

The peak exposure metric was the only formaldehyde metric that showed a significant trend ($P = 0.036$). Peak formaldehyde exposures were divided into ≤ 8.75 mg/m^3, > 8.75–11.6 mg/m^3 and ≥ 11.6 mg/m^3, where the OR was 2.9 (95% CI 0.9–9.8), 2.0 (95% CI 0.6–6.6) and 2.9 (95% CI 0.9–9.5), respectively. The trend was not statistically significant in the cumulative formaldehyde exposure, the average formaldehyde intensity while embalming and the 8-hour time-weighted intensity group. Only the highest cumulative formaldehyde exposure group (> 11 566 mg/m^3-hours) had a statistically elevated OR of 3.1 (95% CI 1.0–9.6). Except for this, the ORs were elevated (2.0–2.9) and very similar within each of the metrics, but none was significantly increased.

Also, in each of the metrics, none of the trend tests within the formaldehyde groups themselves was statistically significant. It is noted that the overall picture was similar to that in the first analysis except for the fact that the ORs fell by one third in this analysis, where a higher number of case subjects were available in the control group. Only one significant OR appeared in the formaldehyde exposure metrics, which was in strong contrast to the 10 significantly elevated ORs in the first analysis.

It is noted that there is a lack of exposure-dependent differences in OR within the different formaldehyde exposure levels in the different metrics. A lack of exposure-dependent effect could be due either to an inappropriate exposure assessment or to a lack of causality between formaldehyde exposure and myeloid leukaemia; the reference groups contained a low number of case subjects. The method of formaldehyde exposure has limitations, as the estimates were predicted by means of interviews and mathematical modelling rather than being based on measured exposures. Also, it is mentioned by the authors that the peak model was not validated. On the whole, this study cannot be used for risk assessment as it does not provide a convincing exposure–response relationship.

Comparison of the Zhang et al. *(156)* and the Hauptmann et al. *(157)* studies reveals some differences. The Zhang et al. study suggests an effect on all progenitor cells that results in decreased production of lymphocytes, granulocytes, platelets and red blood cells. Similar results were obtained from the in vitro cell cultures with different progenitor cell lines. In the Hauptmann et al. study, the effect was selective at the myeloid progenitor line. Overall, these studies have very high exposure intensities and thus do not contradict the fact that lymphohaemat-

opoietic malignancies are not observed at lower levels, as derived from the 2003 study by Hauptmann et al. *(177)* and its re-analysis by Marsh & Youk *(187)*.

The meta-analysis based on the highest exposure levels reported that formaldehyde caused leukaemia and especially myeloid leukaemia *(180)*. Three hypotheses were proposed. First, formaldehyde could be transported by the blood to the bone marrow, where it could cause initiation in a stem or progenitor cell. Second, as a portion of the bone marrow stem and progenitor cells circulate in the peripheral blood, they may be initiated by formaldehyde absorbed into the blood. Third, initiation of the primitive pluripotent stem cells presented within the nasal mucosa could occur, followed by transport to the bone marrow. Similar arguments were analysed by Pyatt et al. *(173)* and the two first hypotheses were not considered likely owing to the negligible amount of formaldehyde reaching the blood. However, nasal (portal-of-entry) effects caused by high formaldehyde exposure levels could be a plausible mechanism for Hodgkin's lymphoma. However, this was not consistent with the Zhang et al. meta-analysis *(180)*. In summary, potentially offending levels can be considered to be in the range where formaldehyde has shown nasal effects in rats, as no lymphohaematopoietic malignancies were observed with mean exposures below 0.63 mg/m^3 and peak exposures below 2.5 mg/m^3, if caused by formaldehyde at all.

Prediction of nasal cancer

Formaldehyde can induce squamous cell carcinoma of the nasal cavity in rats. As a nasal effect would be consistent across species, it is considered the key to setting an indoor air guideline for carcinogenic effects of formaldehyde. The NOAEL approach for setting a guideline value is based mainly on the strongly non-linear relationship between formaldehyde exposure and development of squamous cell carcinoma in rats, largely corroborated by epidemiological studies. This approach accepts that the fall-off of the carcinogenic effect is so rapid that the observed NOAEL resembles a true NOAEL. Accepting these arguments, an indoor air guideline value can be set by dividing the appropriate NOAEL by one or more assessment factors *(159)*. This approach considers the NOAEL for squamous cell carcinoma in rats (2.5 mg/m^3), the NOAEL for nasal cytotoxicity in rats (1.25 mg/m^3) and the potential development of malignancies in humans, which have not been encountered at mean exposures below 0.63 mg/m^3 and peak exposures below 2.5 mg/m^3 formaldehyde.

To obtain a deeper knowledge and thus a better risk assessment, a biologically motivated model has been developed that models exposures by computational fluid dynamics and the development of cancer from a two-stage clonal growth model *(17,167,188)*. Formaldehyde was assumed to act as a direct mutagen with the effect considered proportional to the concentration of the pro-mutagenic DPX lesion. The DPX formation is considered linearly related to the formaldehyde concentration; the linear relation between formaldehyde and DPX concen-

trations can be considered a worst-case scenario in the low-dose range. At high concentrations, the model includes that cytolethality is followed by cell proliferation. Mutations are considered to occur during cell division, and a tumour cell arises when an initiated cell (modelled by DPX levels) acquires a second mutation *(17,167)*. The relationship between formaldehyde exposure and the average cell division rate was J-shaped in rats. The rapid increase in cell proliferation occurred at a level that was not significantly different from a threshold model with a NOAEL set above 2.5 mg/m^3 *(167)*. The two-stage clonal growth model was shown to predict nasal tumours in rats using a lifetime cumulative probability of squamous cell carcinoma with 13 animals with squamous cell carcinoma among 7684 control rats from the U.S. National Toxicology Program historical control database, and where several of the parameters were estimated from the best fit of the model to the experimental data.

The biologically motivated model was extended to humans and took into account that humans are oronasal breathers *(17,188)*. For the general population, the predicted additional risk of upper respiratory tract cancer for non-smokers, associated with an 80-year continuous exposure to 0.125 mg/m^3 formaldehyde, was about 2.7×10^{-8} *(17)*. The additional risk was estimated to be 10^{-6} or less for non-smokers exposed continuously to 0.25 mg/m^3 formaldehyde *(188)*.

The robustness of the model has been challenged by sensitivity analyses *(189–191)*. Thus, the estimate is sensitive to the DPX half-life in the nose *(190)*; the DPX half-life was accepted as 1.78 hours in the 2003 study by Conolly et al. *(167)* that was based on in vivo rat studies, but it was assumed to be 12.3 hours in the sensitivity analysis *(190)* on the basis of the half-life in immortalized cell lines *(192)*. The estimated risks were sensitive to the incidence of squamous cell carcinoma in the rat control group data *(189,190)* and to the data used for rates of nasal cell replication and death *(189,191)*. For example, the instability of the estimates was seen when the current control group, comprising no squamous cell carcinoma among 341 controls, was used *(189)*, although this frequency is in overall agreement with what would have been expected from the cumulative group by proportional scaling (0.57/341). Overall, the sensitivity analyses highlight the limited possibility of predicting risks from the rare events in the unexposed control group.

The importance of the replication rate of the initiated cell was addressed *(189,191)*. Introducing a minor arbitrarily selected increase in cell division rate by formaldehyde exposure and using the entire historical control group of rats, the predicted human risk of respiratory cancer by the age of 80 years from lifetime exposure varied from about 0.02 to about 1 at 0.1 ppm formaldehyde. Thus, the sensitivity analysis showed that the assumed cell division rate of the initiated cell has a tremendous effect on the predicted risk. This led to the conclusion that the Conolly et al. model *(175)* is not reliable for estimating human risk, irrespective of whether the predictions by Crump et al. *(193)* are at odds with human

epidemiology, which was the main point of critique of the sensitivity analyses *(194)*.

The 2004 estimate of Conolly et al. *(188)* has to be taken cautiously. It is not an upper boundary ("worst-case consideration"), which can reach values – depending on the assumptions in the sensitivity analysis – that are incompatible with epidemiological findings. Beside the key event of cell proliferation in formaldehyde-induced nasal cancer identified in animal studies, the estimates by the International Programme on Chemical Safety *(17)* and Conolly et al. *(188)* qualify the discussion about the size of the formaldehyde-induced risk as well as providing input to the selection of the assessment factor in the NOAEL approach.

A recent model study showed that formaldehyde exposure of children would result in less DPX formation than it would in adults exposed at the same level *(154)*. Consequently, children are not expected to be more sensitive to any carcinogenic effect of formaldehyde than adults and are thus not considered separately in the further evaluation.

Health risk evaluation

Exposure evaluation

The major exposure route for formaldehyde is inhalation. Although concentrations above 0.2 mg/m^3 may be encountered in new or renovated buildings, in new furnishings and at hot and humid times of the year, levels on the average are less than 0.05 mg/m^3 in homes and about half that in public buildings (Table 3.4). The most important way to control the formaldehyde concentration is the air exchange rate and the use of low-emitting materials and products. Environmental tobacco smoke and ozone-initiated reactions of alkene compounds may

Table 3.4. Mean exposure concentrations of formaldehyde in various environments, sampled over several days

Source	Concentration (mg/m^3)
Outdoor air	
General	< 0.01
Highly urbanized or industrial areas	0.02
Indoor air	
General	0.01–0.1
Homes	
General	< 0.05
Range	0.005–0.25
Schools/Kindergartens	
General	< 0.05
Range	0.002–0.05
Public buildings	
General	< 0.025
Range	0.005–0.15

contribute to temporary peak levels. Outdoor concentrations are considerably lower, except in some major cities.

Formaldehyde is a normal component of blood. Exposure to 2.4 mg/m^3 did not increase the blood level and exposure to 0.5 mg/m^3 did not result in an increase in urinary formate excretion due to rapid local metabolism *(1,37,43)*.

Critical health outcomes

Effects of formaldehyde in indoor air are generally expected to be limited to effects at the site of contact, specifically the eyes and nasal and upper airways. Effects are due to direct reactions with formaldehyde itself and do not appear to require metabolism.

Non-cancer

The acute symptom of formaldehyde at indoor exposure concentrations is sensory irritation of the eyes and upper airways. Human exposure studies indicate that 0.63 mg/m^3 is the threshold for trigeminal stimulation of the eyes (e.g. increased blink frequency) and 0.38 mg/m^3 is the threshold for subjective sensory irritation.

In general, the concentration perceived by the olfactory system is lower than that triggering sensory irritation of the eyes and airways, and people may therefore report symptoms at levels below its sensory irritation threshold.

Irritation effects of formaldehyde are not cumulative, based on the reversibility of the chemical reactions of formaldehyde-induced irritation and the lack of detectable accumulation of DNA protein cross-links during repeated exposures.

There is no evidence indicating an increased sensitivity to sensory irritation to formaldehyde among people often regarded as susceptible (asthmatics, children and older people).

Although some studies suggest that formaldehyde plays a role in airway sensitization, an association between formaldehyde and lung effects or sensitization in children have not been convincing owing to confounding factors in the studies, including exposure to traffic-related co-pollutants.

Lung function remains unaltered in adults at exposures below 1 mg/m^3 formaldehyde.

Cancer

Formaldehyde can induce squamous cell carcinoma of the nasal cavity in rats and nasopharyngeal cancer in humans. Long-term exposure to 7.5 mg/m^3 formaldehyde and above caused squamous cell carcinoma of the nasal cavity of rats with a non-linear, biphasic concentration–response relationship having the break point at or above 2.5 mg/m^3. In humans, no excess nasopharyngeal cancer has been observed at mean exposure levels at or below 1.25 mg/m^3 and with peak exposures below 5 mg/m^3.

Exposure to formaldehyde has been suspected of leading to lymphohaematopoetic malignancies. However, most long-term inhalation carcinogenicity studies in rats, mice and hamsters do not suggest induction of lymphohaematopoetic malignancies by formaldehyde at levels associated with nasal cancer. In humans, the overall conclusions from three meta-analyses, as well as a recent study in embalmers, suggest that formaldehyde may be causally associated with lymphohaematopoetic malignancies. The recent study in embalmers found evidence of myeloid leukaemia but not other haematopoietic malignancies; the 8-hour time-weighted average formaldehyde intensity was 0.125–0.25 mg/m^3, the average formaldehyde intensity while embalming was about 1.9–2.25 mg/m^3, and peak exposure was about 10–13 mg/m^3. This suggests that an effect on bone marrow or blood progenitor cells is possible at high exposure concentrations. However, since exposure to formaldehyde concentrations up to 2.5 mg/m^3 has negligible influence on the endogenous formaldehyde blood level, protection against nasal cancer should also protect against leukaemia.

Relevance for health of indoor air exposure

The major exposure route of formaldehyde is inhalation from indoor sources. Formaldehyde is a normal component of blood. Exposure of humans to 2.5 mg/m^3 formaldehyde did not increase the blood levels and exposure to 0.5 mg/m^3 did not result in an increase in urinary formate excretion due to rapid metabolism. This suggests that formaldehyde levels normally encountered in indoor air, not exceeding 0.2 mg/m^3, are not expected to increase internal organ exposure.

Conclusions of other reviews

Regulatory agencies in many countries have established guideline values for concentrations of formaldehyde in indoor air. IARC has classified formaldehyde as a human carcinogen (Group 1) based on sufficient epidemiological evidence of nasopharyngeal cancer, and a recent IARC working group also found sufficient evidence for myeloid leukaemia.

Guidelines

An indoor air guideline for formaldehyde is appropriate because indoor exposures are the dominant contributor to personal exposures through inhalation and indoor concentrations may be high enough to cause adverse health effects.

The lowest concentration reported to cause sensory irritation of the eyes in humans is 0.38 mg/m^3 for four hours. Increases in eye blink frequency and conjunctival redness appear at 0.6 mg/m^3, which is considered equal to the NOAEL. There is no indication of accumulation of effects over time with prolonged exposure.

The perception of odour may result in some individuals reporting subjective sensory irritation, and individuals may perceive formaldehyde at concentrations

below 0.1 mg/m^3. However, this is not considered to be an adverse health effect. The NOAEL of 0.6 mg/m^3 for the eye blink response is adjusted using an assessment factor of 5 derived from the standard deviation of nasal pungency (sensory irritation) thresholds, leading to a value of 0.12 mg/m^3, which has been rounded down to 0.1 mg/m^3. Neither increased sensitivity nor sensitization is considered plausible at such indoor concentrations in adults and children. This value is thus considered valid for short-term (30-minute) duration, and this threshold should not be exceeded at any 30-minute interval during a day.

Thus, a short-term (30-minute) guideline of 0.1 mg/m^3 is recommended as preventing sensory irritation in the general population.

There is sufficient evidence that formaldehyde causes nasal cancer in animals and nasopharyngeal cancer in humans with a non-linear, biphasic concentration–response relationship. Carcinogenicity studies in rats, mice and hamsters do not show a consistent association between formaldehyde and lymphohaematopoetic malignancies. Associations between exposure to formaldehyde and nasopharyngeal malignancies and leukaemia in humans are limited to high exposure concentrations.

Increased cell proliferation due to cell damage is considered a key mechanism for the development of nasal malignancies following exposure to formaldehyde. Overall, indoor air effects of formaldehyde are expected to be limited to the site of contact, generally the nasal and upper airways. Increasing cell proliferation in the nasal mucosa of rats occurs at concentrations at and above 2.5 mg/m^3 formaldehyde. The NOAEL for cell proliferation is 1.25 mg/m^3 for long-term exposures.

Thus a threshold approach to setting a guideline for cancer effects is appropriate. Starting with the NOAEL of 1.25 mg/m^3, assessment factors are applied. An interspecies assessment factor of 3 is proposed because the effect is local (non-systemic) and directly due to formaldehyde itself; for inter-individual variation, an assessment factor as low as 2 is proposed because sensitivity differences are not seen among different populations (asthmatics, children and older people). This would lead to a proposed guideline of 0.21 mg/m^3 for the protection of health for long-term effects, including cancer.

An alternative approach was taken by several other groups, using a biologically motivated model. Their assessments led to a predicted additional risk of 2.7×10^{-8} for continuous lifetime exposure to 0.125 mg/m^3 and a predicted additional risk of 10^{-6} or less for non-smokers continuously exposed to 0.25 mg/m^3.

These two assessments (using a NOAEL/assessment factor approach and estimates from the biologically motivated models) yield similar results, with values of approximately 0.2 mg/m^3. These values are above the guideline for short-term effects of 0.1 mg/m^3. Thus use of the short-term (30-minute) guideline of 0.1 mg/m^3 will also prevent long-term health effects, including cancer.

The use of low-emitting building materials and products, and preventing exposures to environmental tobacco smoke and other combustion emissions, will

minimize exposure-related risk. In addition, ventilation can reduce indoor exposure to formaldehyde.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome for guideline definition

Sensory irritation.

Source of exposure–effect evidence

Experimental study reporting conjunctival redness and increases in eye blink frequency at a four-hour exposure of 0.63 mg/m^3 considered as the NOAEL *(79)*. This was adjusted using an assessment factor of 5 derived from the standard deviation of nasal pungency (sensory irritation) thresholds, leading to a value of 0.12 mg/m^3, which has been rounded down to 0.1 mg/m^3.

Supporting evidence

- Several reviews on sensorial irritation at exposure levels between 0.15 and 1.25 mg/m^3 *(66,67,77)*.
- 12 controlled, mostly double-blind studies on respiratory effects at exposures of 0.08–11.2 mg/m^3 *(78–89)*.

Results of other reviews

IARC: Group I (known human carcinogen) *(1,155,186)*.

Guidelines

0.1 mg/m^3 (30-minute average concentration).

Comments

- The short-term guideline will also prevent effects on lung function as well as long-term health effects, including nasopharyngeal cancer and myeloid leukaemia.
- No change in the guideline as compared to *Air quality guidelines for Europe*, 2nd ed.

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4. Naphthalene

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General description

Naphthalene (CAS Registry Number 91-20-3; molecular formula $C_{10}H_8$) is a white crystalline powder with a characteristic odour (of mothballs). It is a two-ring aromatic hydrocarbon isolated from coal tar. Synonyms used are antimite, naphthalin, naphthaline, naphthene and tar camphor. Naphthalene is the most volatile polycyclic aromatic hydrocarbon (PAH) with a gas-phase part of 90–100%, and has a relatively short half-life of 3–8 hours in the atmosphere. Its physicochemical properties are as follows *(1–7)*: molecular weight 128.17 g/mol; melting point 80.2 °C; boiling point 218 °C; relative vapour density 4.42g/cm^3 at 20 °C and 1 atm; vapour pressure 10 Pa at 25 °C; and diffusion coefficient 7.20×10^{-2} cm^2/s at 298 K. It is soluble in alcohol and acetate but not in water.

Conversion factors

At 760 mmHg and 20 °C, 1 ppm = 5.331 mg/m^3 and 1 mg/m^3 = 0.188 ppm; at 25 °C, 1 ppm = 5.241 mg/m^3 and 1 mg/m^3 = 0.191 ppm.

Sources and pathways of exposure

Naphthalene is produced from coal tar fractions by distillation and crystallization. It is used as feedstock in the manufacture of phthalic anhydride for the synthesis of phthalate plasticizers and synthetic resins. It is also used as feedstock for naphthalene sulfonic acids often used in the production of plasticizers for concrete, as ingredients for plasterboards, as dispersants in synthetic and natural rubbers and as tanning agents in the leather industry. Naphthalene is also used in paints and in the production of the insecticide carbaryl, used in home yards and gardens. Still predominant in the exposure of consumers worldwide is the production and use of crystalline (pure) naphthalene as a moth repellent and disinfectant. Its use as a solid block deodorizer for toilets is also reported. Wood smoke, fuel oil and gasoline also contain naphthalene. The major constituent of creosote, used for timber impregnation, is naphthalene and its alkyl homologues.

Outdoor naphthalene sources mainly originate from fugitive emissions and motor vehicle exhaust. Spills to land and water during the storage, transport and disposal of fuel oil and coal tar are released to the atmosphere by volatilization,

photolysis, adsorption and biodegradation. Usual indoor sources of naphthalene are unvented kerosene heaters and tobacco smoke *(8)*.

Outdoor sources can contribute to low levels of indoor naphthalene. The highest indoor concentrations, however, usually orders of magnitude above the outdoor air levels, come from consumer products such as multipurpose solvents, lubricants, herbicides, charcoal lighters and hair sprays, unvented kerosene heaters, tobacco smoke, rubber materials and – most importantly – naphthalene insect repellents (mothballs) used to protect textiles stored indoors in closets (although this use has decreased, mainly in western Europe).

It is assessed that the primary route of exposure is inhalation, especially in the vicinity of heavy traffic, petrol stations and oil refineries. Although inhalation is the major route of the total human exposure to naphthalene, dermal exposure is not to be neglected. Preuss et al. *(9)* assessed the total daily naphthalene intake from air, food and house dust (including soil) at 1.127, 0.237 and 0.235 μg/kg per day, respectively, for a 70-kg adult. Since people spend most of their time indoors, inhalation of indoor air plays the major role in human total exposure to naphthalene.

Indoor concentrations and exposures

There is limited information available in the literature on indoor air concentrations and personal exposure levels of naphthalene. In Europe, two large-scale population-based studies, EXPOLIS *(10)* and the German Environmental Survey (GerES) *(11)*, provide useful data on indoor air exposure and outdoor air concentrations of naphthalene. Some other studies have been reviewed in the course of the INDEX project *(12,13)*. Results from some studies carried out in and outside Europe are summarized in Table 4.1 and are discussed below.

In Europe, indoor concentrations and personal exposures are usually low, typically below 1–2 μg/m^3 *(14)*. In a large-scale study representative of the Federal Republic of Germany before reunification (n = 479), a mean naphthalene concentration of 2.0 μg/m^3 in residential indoor air within a range of individual samples from 0.7 to 14 μg/m^3 was reported *(9)*. In a follow-up study, 555 dwellings in 150 cities were monitored between May 2003 and May 2006 (child's bedroom; passive sampling for one week) *(15)*. The indoor concentration of naphthalene was below the detection limit (1 μg/m^3) in 93% of the houses. The median concentration and 90th percentile were below the detection limit, whereas the 95th percentile and maximum value were respectively 1.2 and 4.9 μg/m^3.

In contrast to this, naphthalene exposures in Athens were found to be remarkably higher. Here, the USEPA's 2006 inhalation reference concentration of 3 μg/m^3 *(16)* and the INDEX project's long-term guideline value of 10 μg/m^3 *(13)* were exceeded in every personal exposure, and the mean and median concentrations were 54.0 and 22.6 μg/m^3, respectively. In Athens, there were five

participants whose personal exposures were considerably higher than the rest of the population and ranged from 74 to 469 μg/m^3. Indoor concentrations were even higher, ranging from 114 to 989 μg/m^3, respectively *(14)*.

Few data could be found on naphthalene concentrations in public spaces, transport and schools, and these are summarized in Table 4.1. Only two European studies carried out in Germany deal with schools and hospitality venues, respectively. In addition, some non-European studies were reviewed.

In Schleswig-Holstein, 285 classrooms from 105 schools and day-care centres were investigated for VOCs (active sampling) between July 2005 and February 2007 *(17)*. In 216 classrooms (76%), the naphthalene concentration was below the detection limit of 1 μg/m^3. The median concentration, 90th and 95th percentiles and maximum value were respectively <1.0, 1.0, 3.7 and 22 μg/m^3. Naphthalene was not measured in a previous campaign carried out in Schleswig-Holstein in 1990–1993, so no comparison can be provided.

Active sampling of indoor air was conducted for 4 hours during the main opening hours in 28 hospitality venues in the cities of Augsburg and Munich, from April 2005 to May 2006 at a time when smoking was allowed *(18)*. Median levels of naphthalene were 80.0 μg/m^3 in restaurants and cafés (n = 11), 59.0 μg/m^3 in pubs and bars (n = 7) and 98.5 μg/m^3 in discotheques (n = 10).

In Table 4.1, the naphthalene concentrations vary widely between 0.036 and 143.9 μg/m^3. Although it would be more appropriate to differentiate between the data measured in different ways, such a differentiation is not reflected in Table 4.1.

In the studies reviewed in the European INDEX project, residential indoor concentrations were elsewhere low, typically averaging below 2 μg/m^3, whereas in Athens clearly higher indoor levels were measured, being on average 90 μg/m^3 *(10)*. Personal exposures to naphthalene elsewhere ranged from 1 to 3 μg/m^3 *(10,11)*, whereas in Athens the average exposure was 46 μg/m^3. In general, we can conclude that exposures to naphthalene are usually low in Europe, but in Athens (and presumably also other countries in eastern and southern Europe) remarkably higher indoor levels of naphthalene were present.

Maroni et al. *(19)* reported typical median and 90th percentile naphthalene concentrations in indoor air in Italy of 2 μg/m^3 and 5 μg/m^3, respectively. Kostiainen et al. *(20)* detected slightly lower indoor concentrations in Helsinki, 0.44 μg/m^3 and 1.63 μg/m^3 being the mean and maximum concentrations. Bituminous materials commonly used in the United Kingdom for damp-proofing floors emit naphthalene *(21)*. Naphthalene concentrations up to 970 μg/m^3 were found in homes having an objectionable smell, where a damp-proof membrane had been applied, compared with less than 300 μg/m^3 for control homes *(22)*. Rubber flooring may also emit naphthalene in odorous amounts. In an Italian study, the average indoor naphthalene concentration was 11 μg/m^3 and the maximum level 70 μg/m^3 *(23)*.

In tropical areas, indoor naphthalene concentrations seem to be generally higher. Mean values in Burundi and Taiwan, China were about 30 μg/m^3 *(9)*. Zuraimi et al. *(24)* compared the characteristics of VOCs and the associated factors affecting them in office buildings in Europe (EU) and in Singapore. They found that concentrations of naphthalene were significantly higher (mean and maximum 144 μg/m^3 and 745 μg/m^3, respectively) in Singapore buildings compared to the EU buildings (mean and maximum 6.5 μg/m^3 and 68.5 μg/m^3, respectively, see Table 4.1).

Area-specific emission rates of naphthalene were also significantly higher and ventilation rates significantly lower in Singapore buildings. Higher levels of naphthalene in ETS-free Singapore buildings were associated with human activity.

Jia et al. *(25)* measured VOCs in indoor and outdoor environments in Michigan, United States to assess their health risk drivers. Monitoring was conducted during two seasons inside and outside 159 residences in industrial, urban and suburban cities. Outdoor concentrations were elevated in winter in the suburban community and were highest in the industrial community. Indoor concentrations were higher in the summer. Seasonal changes were small or inconsistent. Indoor levels of naphthalene exceeded the inhalation reference concentration of 3 mg/m^3 in 12% of residences. The highest level measured was 91.7 μg/m^3.

Yu *(26)* pointed out that indoor naphthalene pollution may also be an issue in Chinese archives. The Chinese Government banned the production and sale of mothballs in 1993, but the use of mothballs in archives and libraries is still permitted for the protection of documents and specimens. It was estimated that up to 10–12 mothballs per m^2 were used in a typical Chinese archive, but unfortunately no measurements have been reported for such an environment.

Lu et al. *(27)* modelled the regional distributions and human exposures to naphthalene in southern California. Petrol and diesel engine exhaust, with related vaporization from fuels, were found to contribute roughly half of the daily total naphthalene burden in southern California. Based on their analysis, the mean hourly naphthalene exposure of the population was 0.27 μg/m^3 in the summer and 0.43 μg/m^3 in the winter. Higher exposures are experienced by a fraction of the population. More than one million people were exposed to naphthalene levels greater than 1 μg/m^3 during wintertime and nearly 100 000 were exposed to average concentration exceeding 2 μg/m^3.

Lu et al. *(28)* reported the results of a PAH pollution survey in the air in public places in Hangzhou, China. The most serious PAH pollution was found in indoor air in shopping centres and the least in railway stations. The highest naphthalene concentration (23.5 μg/m^3) was measured in a shopping centre (see Table 4.1). The authors concluded that emissions of 2–4-ring PAHs occurred from indoor sources in shopping centres and supermarkets, whereas 5–6-ring PAHs originated predominantly from outdoor air. In temples, PAHs in indoor air

mainly originated from incense burning. Naphthalene was the largest contributor (62.4%) to the total health risk when risks associated with the inhalation of PAHs were assessed.

To understand PAH generation in kitchens, Zhu & Wang *(29)* surveyed six representative homes and four commercial kitchens in Hangzhou, China. The highest naphthalene concentrations in a commercial kitchen, in a domestic kitchen of a non-smoking family and in a kitchen of a smoking family were 3.0, 2.7 and 9.9 μg/m^3, respectively. Naphthalene was identified as the most predominant PAH, mostly resulting from the evaporation of mothballs used to protect clothes.

Liu et al. *(30)* measured PAHs simultaneously in the indoor and outdoor air of eight homes in Hangzhou, China. Of the 12 PAHs, naphthalene was the most abundant in both indoor (0.122–26.9 μg/m^3) and outdoor air (0.072–25.1 μg/m^3). Both in summer and in autumn, it contributed more than 60% to the sum of PAHs.

Using standard methods, Lin et al. *(31)* studied the role of incense burning on human exposure to 21 PAHs and total suspended particulates (TSP) in and around a temple in Taiwan, China. Indoor mean total PAH, particle-bound PAH and TSP concentrations were 6.26 μg/m^3, 490 μg/g and 1.32 μg/m^3, respectively. Values for outdoor readings were 0.23 μg/m^3, 245 μg/g and 73 μg/m^3, respectively. With respect to concentrations of individual PAHs (particulate + gas phase), the naphthalene concentration was the second highest at 1.26 μg/m^3. The median indoor : outdoor ratio for naphthalene was 8.6. Median values for indoor : outdoor ratios of individual PAHs ranged from 5.7 to 388, which implied that the temple was a significant PAH source. Moreover, the PAH content of the tested stick incense and ash was low. PAH levels inside the temple were much higher than those measured in the vicinity and inside residential houses, and were in fact close to levels measured at a nearby traffic intersection.

Li & Ro *(32)* measured 15 PAHs simultaneously in the indoor and outdoor air of 14 homes in the Taipei urban area during the summer and winter seasons. They reported that indoor PAH concentrations generally exceeded the corresponding outdoor PAH concentrations. In homes using incense, PAHs could be attributed mainly to incense burning. The most abundant PAH found indoors was naphthalene.

In Australia, several studies have been conducted to detect naphthalene but so far no direct indoor naphthalene concentration data have been forthcoming. The only two indoor studies on indoor naphthalene are summarized below.

Zou et al. *(33)* investigated PAH profiles from the combustion of different Australian firewood species in a domestic wood heater in a laboratory. The 16 PAH emission rates obtained varied between 5965 and 11 508 μg/kg for four firewood species and they were mainly emitted in the gaseous phase (91–98.8%). Overall, gaseous naphthalene accounted for up to 69% of total PAHs in the air.

Table 4.1. Naphthalene concentrations in air reported in the reviewed scientific literature

Reference	Country/city	Period	Environment
Residential settings, European studies			
Jantunen et al. *(10)*	Athens	1996–1997	Residences, indoors
	Basel	1996–1997	Residences, indoors
	Helsinki	1996–1997	Residences, indoors
	Milan	1996–1997	Residences, indoors
	Oxford	1998–2000	Residences, indoors
	Prague	1996–1997	Residences, indoors
Jantunen et al. *(10)*	Athens	1996–1997	Personal exposure
	Basel	1996–1997	Personal exposure
	Helsinki	1996–1997	Personal exposure
	Oxford	1998–2000	Personal exposure
	Prague	1996–1997	Personal exposure
Hoffman et al. *(11)*	German survey	1990–1992	Personal exposure
KUS *(15)*	German survey	2003–2006	Residences. indoors
Non-European studies			
Jia et al. *(25)*	Michigan, USA	2004–2005	Residences, indoors Residences, outdoors
Zhu & Wang *(29)*	Hangzhou, China	1999–2000	Domestic kitchen, non-smoking Domestic kitchen, smoking Commercial kitchen
Ohura et al. *(35)*	Shimizu, Japan	2000 2001	Residences, indoors, summer Residences, indoors, winter
Public spaces			
Lu et al. *(28)*	Hangzhou, China	2006	Railway station, indoors Shopping centre, indoors Supermarket, indoors Supermarket, indoors/outdoors Hotel, indoors Temple, indoors Temple, indoors/outdoors
Zuraimi et al. *(24)*	Singapore Europe	2006 2006	Office buildings Office buildings
Heinzow & Ostendorp *(17)*	Germany	2005–2007	Schools
Bolte et al. *(18)*	Germany	2005–2006	Hospitality venues
Lin et al. *(31)*	Taiwan, China	1996	Temple, indoors Temple, outdoors

[a] AM = arithmetic mean, SD = standard deviation, GM = geometric mean, max = maximum value.

Averaging time	No. of samples	Concentration (µg/m³) [a]			
		AM	SD	GM	Max
30 hours	42	83.5	197		
30 hours	47	0.7	0.3		
30 hours	188	0.6	0.5		
30 hours	41	21.0	81.6		
30 hours	40	1.3	1.5		
30 hours	46	2.0	1.9		
48 hours	46	47.1	78.0		
48 hours	50	0.8	0.6		
48 hours	193	0.7	0.2		
48 hours	42	0.8	0.5		
48 hours	49	2.4	2.8		
1 week	113	2.3		2.1	
1 week		< 1			4.9
3–4 days	226 samples	3.5			91.8
3–4 days	252 samples	0.3			4.7
12 hours	3 kitchens	1.8			2.7
12 hours	3 kitchens	5.3			9.9
12 hours	4 kitchens	2.3			3.0
24 hours	25 houses	1.1			
24 hours	22 houses	1.0			
12 hours	2 samples	2.7			
12 hours	2 samples	23.5			
12 hours	2 samples	19.7			
12 hours	20 samples	2.38	0.59		3.5
12 hours	2 samples	16.3			
9 hours	2 samples	16.1			
9 hours	16 samples	4.14	1.98		7.1
–	8 buildings	143.9	93.0		745
–	50 buildings	6.5	4.3		68.5
	105 schools	< 1			22
4 hours	28 venues				
	Restaurants & cafés (11)	80.0			
	Pubs and bars (7)	59.0			
	Discotheques (10)	98.5			
8 hours	6 samples			1.22	
24 hours	6 samples			0.16	

Duigu et al. *(34)* examined PAH composition on the surface films from the glass windows of 18 residential buildings. The results indicated an average naphthalene concentration on the films of 33.7 ± 44.2 ng/m^2.

Comparison of indoor with outdoor concentrations

Average outdoor naphthalene concentrations are low in Europe, ranging typically from 1 to 4 μg/m^3 *(10)*. Even lower outdoor levels, below 1 μg/m^3, have been reported in Taiwan, China and the United States (see Table 4.1). The outdoor concentration of naphthalene in air is generally lower in rural than in urban areas.

The indoor mean concentration of naphthalene is reported to range up to a maximum of 143.9 μg/m^3, although the majority of studies report average naphthalene indoor levels below 10 μg/m^3.

Table 4.1 shows the naphthalene air concentrations reported in a number of scientific publications. However, several different sampling techniques were used in these studies. For example, Ohura et al. *(35)* employed glass fibre filters and XAD-2 resin for particulate and gaseous naphthalene sampling, respectively, while the EXPOLIS project utilized only a Tenax TA tube to collect both phases of naphthalene. It was also reported by Lin et al. *(31)* that polyurethane foam had been used to sample gas-phase naphthalene with other vapour PAHs.

Biomarkers of human exposure to naphthalene

Urinary 1- and 2-naphthol are well-established human biological exposure indices to evaluate the exposure to naphthalene of workers as well as the general population. Median 1-naphthol concentrations found in non-smokers without known occupational exposure range from 1 to 5 μg/l urine and median 2-naphthol concentrations from 1 to 3.6 μg/l *(36)*. Smokers show significantly higher naphthol concentrations *(9,36)*.

Both 1- and 2-naphthol were used to check the impact of genetic polymorphisms on naphthalene metabolism *(37–39)*. Urinary 2-naphthol concentrations were higher in smokers with the CYP2E1 genotypes c1/c2 or c2/c2 than in smokers with the more common c1/c1 genotype. Higher concentrations of 1- and 2-naphthol were found in the urine of smokers deficient in glutathione S-transferase M1. In recent studies, 2-naphthol was used as a biomarker to evaluate polymorphisms in patients with lung cancer or oral squamous cell carcinoma *(40,41)*.

A glucose-6-phosphate dehydrogenase deficiency has been suggested to lead to an increased susceptibility to haemolytic anaemia in children and newborn infants exposed to naphthalene, but exposure levels of naphthalene were not estimated in most reports. Haemolytic anaemia observed in neonates could also be explained by a lower ability to metabolize naphthalene and eliminate naphthalene metabolites. In a Nigerian study, five neonates presenting with jaundice or

tetanus showed very high urinary 1-naphthol concentrations *(42)*. Three of them were deficient in glucose-6-phosphate dehydrogenase. In this group, the 1-naphthol concentrations ranged from 1140 to 11 690 μg/l urine, similar to those of the non-deficient newborn infants (750–9550 μg/l). Such high naphthol concentrations have been reported in occupational settings but not in humans *(9)*.

It is recommended that 1- and 2-naphthol be measured simultaneously, since both metabolites correlate. An elevated level of 1-naphthol alone may be an indicator of an additional exposure, such as to the biocide 1-naphthyl methylcarbamate (carbaryl) or to some hair dyes *(43)*. A study in the Republic of Korea on non-smoking municipal middle-school students showed significant correlations between urinary 2-naphthol concentrations and the daily mean total suspended particulate level estimated for 1–2 days before and for the day of the survey *(44)*.

In a recent study, a method was developed for measuring urinary 1,2- and 1,4-dihydroxynaphthalene *(45)*. Strong correlations were observed among these naphthadiols and both naphthols in urine. Further, the urinary concentrations of 1,2-dihydroxynaphthalene were significantly correlated with the serum concentrations of 1,2-naphthoquinone albumin adducts.

Kinetics and metabolism

Kinetics

There are no published studies that document the precise bioavailability of naphthalene after oral, dermal or inhalation exposure. It is clear from human poisoning cases *(46)*, the exposure of air force personnel to jet fuel containing naphthalene *(47,48)* and numerous animal studies *(49)* that naphthalene can be absorbed by all three routes. In exposed human volunteers, dermal administration of naphthalene resulted in relatively rapid uptake of the parent compound, with peak levels observed in approximately 60 minutes. Calculated partition coefficients demonstrate high partitioning of naphthalene in the fat, while toxicokinetic studies in mice after inhalation exposure and in rats after both inhalation and intravenous administration *(49)* demonstrate rapid clearance from the blood. Very little naphthalene is eliminated unchanged in expired breath, a finding consistent with the results of the physiologically based toxicokinetic analysis suggesting that 88–98% of inhaled naphthalene is eliminated as metabolic by-products.

Very recently, work has been taken up to better understand gender and species differences in upper respiratory tract uptake and in situ metabolism of naphthalene *(50)*. At a flow of 150 ml/minute, upper respiratory tract uptake in female F344 rats exposed to naphthalene concentrations of 5, 21, 53 or 181 mg/m^3 was concentration-dependent, with rates of 56%, 40%, 35% and 28%, respectively. These rates were similar to the uptake observed in male rats (57%, 49%, 37% and 36%, respectively). The concentration dependence of naphthalene uptake in the upper respiratory tract is probably due to nasal metabolism of

naphthalene. A significant reduction of naphthalene uptake was observed after pre-treatment with the inhibitor 5-phenyl-1-pentyne.

Metabolism

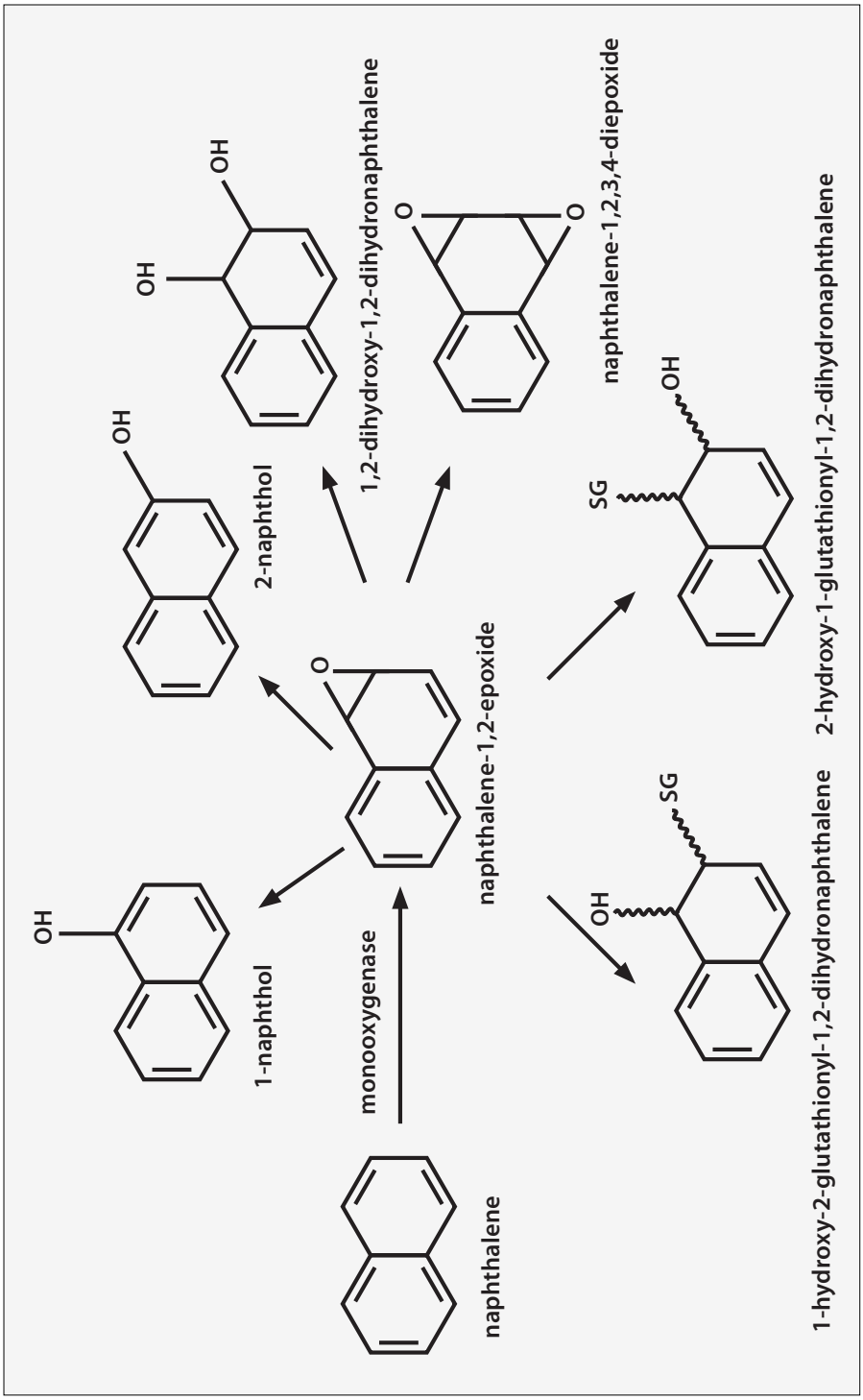
The metabolism of naphthalene to metabolites that can be excreted by mammals occurs as a multi-step process involving both initial oxygenation reactions and subsequent conjugation. The first step in metabolism involves the formation of an unstable 1,2-epoxide (Fig. 4.1) that can be catalysed by several cytochrome P450 monooxygenases. Several (e.g. 2A13, 2E1, 2F1 and 2F2) can oxidize naphthalene to naphthalene-1,2-epoxide and further to 1,2,3,4-diepoxide. Naphthalene-1,2-epoxide can also be rearranged to 1- or 2-naphthol or be transformed by epoxide hydrolases to dihydroxy-dihydro-naphthalene or by glutathione transferases to glutathionyl derivates.

These monooxygenases are discussed in detail below, since the initial formation of naphthalene oxide is a key step in the downstream toxicological activities associated with naphthalene exposure. A number of further metabolites can be generated directly from the epoxide by both enzymatic and non-enzymatic processes. The cytochrome P450 monooxygenases can biotransform naphthalene to a putative diepoxide or diolepoxide *(51,52)*, microsomal epoxide hydrolases generate a trans-dihydrodiol *(53)* and the glutathione transferases form diastereomeric glutathione conjugates *(54)*, which are eliminated primarily as mercapturic acids *(51,52)*. In water, 1- (major) and 2-naphthol (minor) arise from non-enzymatic rearrangement of the epoxide *(55)*. In human liver microsomal incubations, the calculated V_{max} for the formation of 1-naphthol, 2-naphthol and 1,2-dihydroxy-1,2-dihydronaphthalene were 268, 22 and 2860 pmoles/min per mg protein, respectively *(56)*. Each of these secondary metabolites can undergo further biotransformation and with two of these metabolites (1-naphthol and 1,2-dihydroxy-1,2-dihydronaphthalene), more reactive chemical entities can result. The suspected reactive, toxicologically active metabolites include naphthalene epoxide, naphthalene diepoxide (or diol epoxide), 1,2-naphthoquinone and 1,4-naphthoquinone; the formation and disposition of these will be discussed individually. The primary urinary metabolite eliminated in exposed human populations is 1-naphthol glucuronide *(37,57–59)*. In recent surveys in the United States, this metabolite could be detected in the urine of all 2748 individuals sampled, thus establishing widespread exposure of human populations *(60)*.

Naphthalene-1,2-epoxide

The stability of various aromatic and aliphatic hydrocarbon epoxides varies considerably, which in turn affects the interactions with key cellular macromolecules and overall downstream impact *(61)*. In contrast to aflatoxin epoxide, which has an estimated half life of 1 second in water, naphthalene epoxide has a half-life of 2–3 minutes in water and 11 minutes in solutions of albumin *(62)*. Thus, naph-

Fig. 4.1. The first steps in the metabolism of naphthalene



thalene oxide is sufficiently stable to circulate from organs able to rapidly generate this metabolite to those with lower metabolic rates. While there is some evidence that circulating naphthalene oxide can produce injury in the lung *(62)*, there is a strong possibility that such circulating metabolites may enhance the susceptibility of tissues such as the lung to injury by depleting protective thiols such as glutathione *(63)*.

The importance of regiochemistry and stereochemistry in the biological effects of epoxides and diol epoxides of larger PAHs is well-established. Many PAH-specific P450s show remarkable regioselectivity and stereoselectivity in the metabolites they produce. Similarly, several of the P450s show a high degree of stereoselectivity in naphthalene metabolism. By using N-acetylcysteine to trap reactive naphthalene epoxides, van Bladeren et al. *(64,65)* were able to show that cytochrome P450 2B shows a slight preference for the formation of the (1*S*,2*R*)-naphthalene epoxide (74%) whereas cytochrome P450 1A1 preferentially generates (1*R*,2*S*)-epoxide (73–95%). Studies showing marked differences in the ratio of glutathione conjugates formed in microsomal incubations from mouse lung vs liver demonstrated substantial differences in the stereoselectivity of naphthalene epoxide in target (lung) compared to non-target (liver) tissues *(54)*. Approximately equal rates of formation of the (1*R*,2*S*)- and (1*S*,2*R*)-epoxide were observed in liver microsomes, whereas 10 : 1 ratios of the (1*R*,2*S*)- to (1*S*,2*R*)-epoxide were made in the lung. Similarly, subsequent work using dissected airways from susceptible mice and non-susceptible rats showed the same pattern of stereoselectivity. Metabolism in target regions of the respiratory tract of the mouse resulted in highly selective formation of the (1*R*,2*S*)-epoxide whereas approximately equal proportions of the epoxide enantiomers were made by rat lung airways *(66)*.

This high degree of selectivity in the formation of a single stereoisomer of naphthalene oxide was consistent with 60 : 1 ratios in isomer generation catalysed by cDNA-directed expression of cytochrome P450 2F2 in baculovirus-infected SF-21 cells and with immunolocalization experiments showing that that airway epithelial cells were highly stained. Thus, while it appears that cytochrome P450 2F2 is responsible for the rapid and stereoselective formation of (1*R*,2*S*)-naphthalene oxide, it is not at all clear that the stereoselectivity of this process is relevant to the cytotoxicity associated with naphthalene in the respiratory tract. Although it is possible that the toxicological potency of the naphthalene epoxide enantiomers differ, it seems far more likely that the differential susceptibility of rat and mouse airways and mouse lung and liver are due to the rates of initial substrate turnover. Published data in isolated mouse hepatocytes have shown that the intracellular residence time of the epoxide isomers may differ because of different rates of glutathione conjugation or hydrolysis by epoxide hydrolase, and that this does indeed translate into differential toxicity of these two epoxides *(67)*. However, definitive analysis of the importance of the stereochemistry of

epoxidation of naphthalene in the lung is problematic because of the instability of the epoxide. Short incubations of racemic naphthalene epoxide with dissected airways of both the rat and mouse and in proximal vs distal airways showed very little difference in the rates of formation of glutathione conjugates or in the diastereomers produced. Likewise, there were no discernable differences in the rates of dihydrodiol production between rat and mouse airways that appeared to relate to the species differences in response to naphthalene *(66)*.

1-Naphthol

One of the primary metabolites generated from naphthalene oxide in aqueous solutions is 1-naphthol. The ratios of this rearrangement product to the 1,2-dihydroxy-1,2-dihydronaphthalene (dihydrodiol) are dependent on the rates of formation of the epoxide and the activities of microsomal epoxide hydrolase which are, in turn, species-dependent. 1-Naphthol can be metabolized to protein-reactive metabolites both in vitro *(68,69)* and in vivo *(70)*. Conjugation with sulfate and UDP glucuronic acid results in derivatives that, in many species, constitute major urinary metabolites (see above). 1-Naphthol is a precursor to the formation of 1,4-naphthoquinone, a potential cytotoxic metabolite *(56,71)*. The 1,4-naphthoquinone can stimulate the redox cycle *(72)* and binds covalently to proteins in vitro *(73,74)* and in vivo *(75–77)*.

1,2-Dihydroxy-1,2-dihydronaphthalene

The dihydrodiol, generated through metabolism of the epoxide by epoxide hydrolase, is converted by a dihydrodiol dehydrogenase (aldose reductase) *(78–80)* to the 1,2-dihydroxynaphthalene, which auto-oxidizes to a 1,2-quinone. The 1,2-quinone can bind covalently to protein both in vitro and in vivo *(75–77,81)* and forms depurinating adducts on DNA in vitro *(82)*.

1,2-Naphthalene diepoxide (diolepoxide)

Indirect evidence for the formation of a diepoxide/diolepoxide comes from the isolation of the 1,2,3,4-tetrahydroxytetrahydronaphthalene from urine of naphthalene-treated rats *(83)*.

Glutathione is depleted in murine tissues capable of metabolizing naphthalene in a dose/concentration-dependent fashion after either intraperitoneal administration *(84)* or inhalation *(85)*. Glutathione adducts are generated at both the allylic and benzylic carbons of naphthalene *(54)*. Although the initial studies resolved only three diasteromers, with improved techniques a fourth, minor conjugate has been identified. These glutathione conjugates are eliminated primarily as mercapturic acids and account for 25–35% of a dose of naphthalene administered intraperitoneally to either mice or rats. No species differences were noted in the percentage of dose eliminated as mercapturate *(86)*. In mice, exposure to 319 mg/m^3 resulted in levels of mercapturate in the urine that were similar to

those observed after intraperitoneal administration of 50 mg/kg. It is interesting to note that there appears to be a significant species difference in the amounts of naphthalene eliminated as mercapturates in rodents and non-human primates. In both the chimpanzee *(87)* and the Rhesus monkey *(88)*, an increase in urinary thioether elimination, measured after conjugate hydrolysis with the Ellman assay, was not observed in response to orally administered naphthalene. In comparison, diethylmaleate administration resulted in dose-dependent increases in thioether elimination in both species.

The primary products eliminated in the urine of mice following the intravenous administration of naphthalene glutathione conjugates were mercapturic acids, and accounted for 40–85% of the administered dose *(89)*. Small amounts of cysteine conjugate were measured in the urine. There was a significant difference noted in the metabolic disposition of the benzylic compared to the allylic adducts. Some 15–20% of the administered dose of the 1R-glutathionyl-2R-hydroxydihydronaphthalene was excreted as a thiopyruvic acid derivative.

Enzymes involved in naphthalene metabolism

There is considerable experimental evidence showing that metabolism of naphthalene is required for any of the downstream toxicities associated with this compound in animal models. Thus, a substantial amount of effort has been focused on species comparisons in the rates of formation of naphthalene oxide, as well as on understanding the importance of specific pulmonary cytochrome P450 monooxygenases in the metabolic activation of this agent. The contribution of each of these P450 proteins to the conversion of naphthalene to more biologically active derivatives is dependent not only on the amounts of protein present but also on the catalytic activities of each of the proteins. Unfortunately, quantifying the amounts of each of the cytochrome P450 isoforms present in various subcompartments of the lung is difficult and in only a few cases has purified protein been available as standard *(90)*. More information is available on the catalytic properties of some of the P450 monooxygenases through the use of recombinant proteins. Since the environmental levels of naphthalene are quite low, data on the catalytic efficiencies (K_m) of the individual P450 monooxygenases is also a key to assessments designed to determine whether low-level, long-term exposures are a potential risk to human health. Accordingly, the following sections discuss what is known about the overall rates of metabolism of naphthalene in target and non-target tissues of rodents and primates, along with a discussion of P450s known to metabolically activate this substrate.

Comparative metabolism studies in rodents and primates

There are 50–100-fold differences in the rates of naphthalene metabolism to water-soluble metabolites in microsomal incubations prepared from target and non-target rodent tissues and corresponding tissues of the Rhesus monkey and

human *(91,92)*. In general, the rates of metabolism correlate well with the tissue susceptibility to toxicity. At saturating substrate concentrations, mouse lung (target tissue) microsomal naphthalene metabolism occurs at rates of 15 nmoles/mg microsomal protein per minute, compared to less than 2 nmoles/mg per minute in rat lung (non-susceptible). Likewise, the rates of microsomal naphthalene metabolism in rat olfactory epithelial tissues (highly susceptible to naphthalene) are approximately 16 nmoles/mg per minute *(93)*. In comparison, Rhesus monkey lung microsomes metabolize naphthalene at a rate of 0.15 nmoles/mg per minute. Similar rodent-to-primate differences were observed using more specific approaches, where metabolism was measured in target subcompartments *(66,94)*.

Enzymology of naphthalene epoxide formation

CYP2F. Nagata and co-workers *(95)* purified a cytochrome P450 monooxygenase from mouse liver that metabolized naphthalene rapidly and with high stereoselectivity. The gene was cloned and sequenced *(96)* and had 82% sequence homology to a cDNA that had been cloned earlier from human lung *(97)*.

CYP2F2 (mouse). Naphthalene is metabolized with a high degree of stereoselectivity by recombinant mouse CYP2F2 expressed in either yeast *(96)* or in SF-21 insect cells *(98)*. A very high V_{max} (107 nmoles product/nmole P450 per minute) and low K_m (3 μM) for the metabolism of naphthalene by recombinant CYP2F2 are consistent with the importance of this protein in the metabolic activation and toxicity of naphthalene in mouse lung. The low K_m observed is well below the range of expected tissue concentrations in the lung after inhalation exposure at the 53-mg/m^3 level. N-terminally truncated recombinant human keratinocyte growth factor (DeltaN23_KGF) lowers the expression of CYP2F2 in mice, thus reducing the airway injury of naphthalene *(99)*.

CYP2F4 (rat). Immunocytochemistry with antibodies generated to the mouse 2F *(66)* and northern blot analysis initially failed to demonstrate the presence of a P4502F orthologue in the rat. More detailed investigations uncovered a transcript that had 94% similarity in the deduced amino acid sequence to CYP2F2 *(100)*. cDNA-directed expression of CYP2F in SF-21 insect cells yielded a protein with nearly identical catalytic activities to the mouse orthologue. Thus, the substantial differences in susceptibility of mouse compared to rat lung was not likely to be due to differences in the catalytic differences in metabolism by CYP2F, but rather appears to be related to the amounts of protein present as assessed by immunoblot analysis *(101)*.

CYP2F1 (human)/CYP2F5 (monkey). CYP2F1 has been expressed in a number of different recombinant protein expression systems. Although substantial pro-

tein is produced in the baculovirus-infected SF-21 cells, a P450 spectrum could not be obtained. Similiarly, cDNA-directed expression of CYP2F5 from the Rhesus monkey resulted in protein but no haem incorporation. Both proteins were catalytically inactive *(100)*. Expression of CYP2F1 in lymphoblastoid cells *(102)* resulted in the production of a protein with very low rates of naphthalene turnover (~0.035 nmoles conjugate/min per nmole P450). This rate is less than 0.1% the rate of metabolism observed with the mouse orthologue. The recombinant human CYP2F1 showed slight stereopreference in the generation of (1*S*,2*R*)-naphthalene epoxide.

Other cytochrome P450 monooxygenases. While it is likely that CYP2F is primarily responsible for the metabolic activation of naphthalene in mice, other P450 monooxygenases may play an important role in catalysing the turnover of this substrate in humans. Cho et al. *(56)* have published a very thorough investigation of the catalytic activity of various commercially available cytochrome P450 monooxygenases with naphthalene. Cytochrome P450 2E1 has the lowest K_m of any of the proteins tested (10 μM) with a V_{max} that is 8 pmoles/min per pmole P450 for the formation of 1-naphthol. This is 10-fold lower than the V_{max} for CYP2F2. Cytochrome P450 2E1 has been reported in human lungs based on both immunoblotting and activity assays *(103,104)*. Recent work showing high catalytic activities of CYP2A13 *(105)*, a protein reported in human respiratory tissue *(106)*, suggests that this protein may be important in human metabolism of naphthalene. The K_m and K_{cat} for the formation of 1-naphthol were 36 μM and 143 min^{-1}, respectively. Aryl hydrocarbon receptor-mediated enzymes do not contribute significantly to naphthalene bioactivation in mice *(107)*.

Formation and possible importance of protein-bound metabolites

The concept that reactive metabolite formation can, but does not always, lead to cellular necrosis has been well-established with a number of hepatic, renal and pulmonary toxicants. Early studies with naphthalene showed that reactive metabolites become bound covalently to cellular proteins both in vivo and in vitro in a dose/concentration-dependent manner *(84)*. The irreversible binding of reactive metabolites occurs prior to any signs of cellular degradation, and prior treatment with inhibitors of cytochrome P450 or with glutathione depletors alters the extent and severity of cytotoxicity in concert with the amounts of reactive metabolite bound *(108)*. The binding levels generally correlate with target tissue susceptibility. Although considerable progress has been made in identifying proteins that are adducted by a variety of reactive metabolites, including naphthalene *(109–111)*, it has not been demonstrated that a particular protein adduct (or adducts) results in toxicity. What is clear is that there are commonalities in proteins that are adducted by reactive naphthalene metabolites across species, and the 50–100-fold differences in rates of water-soluble metabolite formation

between rodents and primates are not observed when total reactive metabolite binding is compared. Incubations of dissected airways of Rhesus monkeys with naphthalene resulted in levels of covalent adduct varying from 0.3 nmoles/mg protein in the trachea to 1.2 and 1.4 nmoles/mg protein in the distal airway and parenchyma, respectively *(94)*. Under similar conditions, the rates of formation of reactive metabolites that become bound covalently in dissected airways of mouse lung varied from 0.8 to 3.8 nmoles adduct per mg protein from trachea to distal airway *(112)*. Recent comparisons between rat nasal olfactory epithelium, which is highly susceptible to naphthalene *(93)*, and ethmoid tissues from the Rhesus monkey show nearly identical levels of reactive metabolite formation in in vitro incubations *(111)*.

It is important to note that several naphthalene metabolites are protein-reactive, including the epoxide *(67)* and both the 1,2- and the 1,4-naphthoquinones *(113,114)*. Which (if any) of these metabolites are essential to the steps leading to cytotoxic injury is not clear, nor are the relative contributions of each metabolite to the overall levels of adducts measured. At least in rats and mice, Waidyanatha & Rappaport *(77)* have shown that naphthalene oxide is the primary metabolite that adducts albumin and haemoglobin in both species.

Health effects

Most of the data available on the toxic effects of naphthalene have been derived from animal studies conducted either in vivo or with in vitro preparations *(22,46,115)*. There are reports of acute poisoning through unintentional or suicidal naphthalene exposures in humans but, as described below, the epidemiological data are very scarce regarding dose–response relationships for human health effects with acute, subchronic or chronic exposure by any route. The effects in humans are now discussed, followed by a description of animal data. In some cases, reference will be made to literature in humans, which, based on mechanistic data derived from animals, would be consistent with adverse health effects of naphthalene. It is important to note that the associations and consistency with mechanisms does not constitute proof of health effects and the data may be explained in many other ways. This is especially true when exposure occurred not solely to naphthalene but to mixtures containing naphthalene such as PAH.

Identification of studies

Published studies on health effects of exposure to naphthalene were identified by hand searching references in former reviews by IARC *(115)*, ECB *(22)* and ATSDR *(46)* and completed by electronic search in February and September 2009 in PubMed, using the descriptors "naphthalene" and "health effects", "toxicity", "lung", "epidemiology", "susceptibility", "cancer", "mothballs" or "poisoning". Following the last review, only a few new epidemiological studies and about two

dozen toxicity studies in mammals or in vitro studies were found. We excluded studies that referred to PAHs but were lacking a sufficient description of exposure to naphthalene.

Effects on humans

Acute effects

Many of the case reports of human exposure to naphthalene involve ingestion of mothballs. The most serious effects are reported in individuals with glucose 6-phosphate dehydrogenase deficiency, where haemolytic anaemia is the primary adverse effect. Many of these involve poisoning in paediatric patients *(116,117)*. In a recent survey of 24 paediatric patients admitted to hospital with acute haemolysis, nearly 60% were found to have been associated with naphthalene-containing mothballs *(118)*. In one case report, involving accidental prenatal exposure to mothballs, both the mother and, following birth, her preterm infant presented with haemolytic anaemia and methaemoglobinaemia *(119)*. Follow-up of both mother and child a year later revealed nothing remarkable. The effortless availability and widespread domestic use of naphthalene-containing mothballs may further lead to acute naphthalene poisoning, including the non-accidental ingestion of mothballs *(120)*.

Chronic effects

Very few cases have been documented of chronic naphthalene exposure in humans. Two of the reports purportedly showing a link between laryngeal *(121)* or colon cancer *(122)* with naphthalene exposure have been judged by both the US National Toxicology Program (NTP) *(123)* and IARC *(115)* as being sufficiently poorly controlled to be unreliable. In a population-based case-control study among women in New York State, the increase in risk of non-Hodgkin's lymphoma diagnosed between October 1995 and September 1998 was significantly associated with the household use of mothballs *(124)*. The lack of a dose–response among users, the unknown chemical constituent(s) of the mothballs used (naphthalene or para-dichlorobenzene), and selection and recall bias limit the drawing of firm conclusions.

There is an early report of human cataractogenesis induced by naphthalene in a dye manufacturing facility, which is consistent with subsequent work in animal models (discussed below) *(125)*. Some studies suggest an association between exposure to biomass fuel smoke and cataracts or lens opacity *(126,127)*, but exposure levels of naphthalene associated with these effects have not been estimated. The final case is of a middle-aged woman who had been sniffing mothballs containing naphthalene for more than 30 years *(128)*. The patient presented with signs of peripheral neuropathy and renal failure. Naphthalene was thought to be a possible contributing factor, but these symptoms were also likely to be related to diabetes, hypertension and obesity.

Odour perception

Naphthalene has a mothball-like odour. Published odour thresholds of naphthalene range from 0.0075 to 0.42 mg/m^3 *(129,130)*.

In vitro studies

There are a number of studies indicating that human cells are susceptible to naphthalene metabolites in vitro. Tingle et al. *(69)* used human liver microsomes to generate reactive metabolites from naphthalene, which were subsequently tested for cytotoxicity using peripheral blood mononuclear leukocytes. Cell death was dependent on the presence of NADPH. Inhibition of epoxide hydrolase with trichloropropylene oxide enhanced toxicity at all three concentrations of naphthalene studied (1, 10 and 100 μM). Interestingly, no effects were noted in sister chromatid exchange (SCE) frequency in cells incubated with human liver microsomes, with or without NADPH. An increase in SCE frequency was observed with the positive control, aflatoxin B_1. Later studies that tested the toxicity of naphthalene, 1-naphthol, 1,2- and 1,4-naphthoquinone and naphthalene oxide on human mononuclear leucocytes and lymphocytes showed that both quinones resulted in concentration-dependent cytotoxicity and that 1-naphthol required the presence of an activating system to generate metabolites that were cytotoxic *(131)*. The dihydrodiol was not cytotoxic at concentrations up to 100 μM. Similarly, both quinones resulted in increased numbers of SCEs. More recent work with cord blood showed that naphthalene at high concentrations (500 μM) increased the expression of several antiapoptotic proteins, including BCl-2 *(132)*. Similarly, three naphthalene metabolites (1- and 2-naphthol and 1,4-naphthoquinone) produce concentration-dependent decreases in the clonogenicity of colony-forming units, granulocyte-macrophage (CFU-GM) in cord blood from both male and female donors. Ranked IC_{50} (concentrations required to decrease clonogenicity by 50%) values for these metabolites were 2-naphthol > 1-naphthol > 1,4-naphthoquinone *(133)*. The reported IC_{50} for the quinone was 0.5–1.9 μM. Naphthalene was inactive at concentrations as high as 5 mM.

Overall, these studies indicate that human liver microsomes are capable of metabolically activating naphthalene to derivatives that are cytotoxic to human cells, and that the known metabolites of naphthalene are capable of producing cytotoxicity when added to cells. With some of these metabolites, cytotoxicity is observed at relatively low levels.

Effects on experimental animals and in vitro test systems

Animal studies in vivo

Acute/subacute studies. Toxicity to the respiratory tract is the most notable lesion associated with naphthalene exposure in animals but the subcompartments of the respiratory tract targeted by this compound depend highly on the species, the age and sex of the animals and the route of administration (Table 4.2). Ocular

injury has also been observed in a number of species and the mechanisms for this appear to be well-established.

Work examining the acute toxicity of naphthalene administered by inhalation has recently been completed *(134)*. Four-hour exposures to concentrations as low as 11 mg/m^3 resulted in detectable Clara cell injury in the proximal airways of adult male mice. Injury was concentration-dependent and proceeded from the proximal, most sensitive airways to distal and less sensitive airways. As the concentration increased, injury became more severe in the proximal airways and extended down into more distal portions of the lung. At 53 mg/m^3, significant cell disruption was noted at all airway levels in mice. In contrast, airway epithelial injury was not observed at any exposure concentration up to the highest concentration tested (585 mg/m^3). Substantial injury of nasal olfactory epithelium in Sprague-Dawley rats was observed following naphthalene inhalation at low exposure concentrations (18 mg/m^3 for four hours) *(93)*. More recently, olfactory epithelium necrosis occurred in SD and F344 rats after a single six-hour whole-body exposure to 5 mg/m^3 naphthalene *(135)*. Lesions of the respiratory and olfactory epithelium were observed at the 53- and 160-mg/m^3 exposure concentrations in male and female F344 and SD rats. The preliminary report indicates that SD rats appear to be more sensitive and that the threshold for injury may be much lower – in the 0.5–1.6-mg/m^3 range. In a subacute study that was not published but reviewed by the European Chemicals Bureau *(22)* and retained as valuable information in the INDEX project *(13)*, male and female Sprague-Dawley rats were exposed nose-only to 0, 5, 17, 55, 153 or 372 mg/m^3 vaporized naphthalene (D. W. Coombs, unpublished data, 1993). In the nasal olfactory epithelium, local lesions with signs of proliferative repair were observed at all doses down to 5 mg/m^3. The findings were similar to those from a subchronic study (see below).

The olfactory region of the nose is also sensitive to naphthalene after intraperitoneal administration in both the mouse and the rat *(136)*. The rat nasal olfactory epithelium is more sensitive than the mouse epithelium: significant necrosis was observed in the rat at intraperitoneal doses of 200 mg/kg, whereas injury in the mouse was not observed until 400 mg/kg. Finally, more recent studies investigating the sex and strain differences in susceptibility to naphthalene toxicity indicate that female Swiss Webster mice are more susceptible to the cytotoxicity of naphthalene than males *(137)*. These differences were detected primarily by differences in uptake of vital dye and consisted of earlier and more extensive injury following a 200-mg/kg dose. Few differences were noted in the extent of initial injury in different mouse strains *(138)*. As discussed below, the chronic bioassay investigating the possible neoplastic effects of naphthalene showed a sex difference in susceptibility: female mice showed a slight increase in bronchioloalveolar neoplasms over the control, whereas in males there was no effect.

In addition to the lesions observed in the nose, the pulmonary toxicity of naphthalene has been studied extensively by a number of laboratories

(136,137,139,140). More recently, naphthalene has been used as a selective Clara cell toxicant to evaluate progenitor cells involved in the repair of the airway epithelium *(141–143)* and to determine whether co-exposures to pulmonary toxicants alter either the initial response or the later repair of the injury *(144,145)*. Pulmonary regenerative response to naphthalene-induced lung injury in mice depends on gender, showing a significantly greater cell proliferation in female compared to male mice *(146)*. Clara cells lining the airway epithelium of the mouse are the primary target cells for naphthalene toxicity, irrespective of the route of administration. After parenteral administration of low doses of the compound, the only tissue affected is the respiratory tract (Table 4.2). Hepatic necrosis is not observed at any dose of naphthalene tested, while proximal tubular cells of the kidney are injured only in some mouse strains and only at very high doses (400 and 600 mg/kg) *(147)*. Swelling of Clara cells in terminal airways is detected in mice at intraperitoneal doses as low as 50 mg/kg. In contrast, in rats even at LD_{50} intraperitoneal doses (1600 mg/kg) airway Clara cells appear normal. Slight swelling of Clara cells in the hamster is observed at the LD_{50} intraperitoneal dose (800 mg/kg) *(136,140)*. In all of the species tested, no injury to the alveolar type I or II cells has been observed. Recently, naphthoquinone was shown to enhance an antigen-related airway inflammation with goblet cell hyperplasia in mice *(148)*. Following an intratracheal application of naphthoquinone to ICR mice for six weeks, airway hyperresponsiveness was enhanced by naphthoquinone in the presence or absence of an antigen *(149)*.

In contrast to the Clara cell toxicity observed after single doses of naphthalene, multiple daily treatments with naphthalene by either the intraperitoneal or inhalation routes result in tolerance to high challenge doses of the compound *(150–152)*. Although acute 200-mg/kg doses intraperitoneally result in substantial injury to Clara cells of mice, treatment for seven days at this same dose caused slight hyperplasia of the epithelium but no frank necrosis or vacuolation. Seven daily treatments with 200 mg/kg naphthalene markedly attenuated the toxicity observed following a 300-mg/kg challenge dose given 24 hours after the last 200-mg/kg dose in comparison to corn-oil-treated controls challenged with 300 mg/kg naphthalene (Table 4.2). As the time between the last 200-mg/kg dose and the challenge dose was extended from 24 to 96 hours, the lungs regained a portion of their sensitivity to the 300-mg/kg challenge dose. Later studies using inhalation exposures at 80 mg/m^3 showed similar effects *(152)*. Tolerance to repeated naphthalene exposures does not appear to be related to changes in the metabolic activation of naphthalene but rather to faster turnover of glutathione associated with upregulation of γ-glutamylcysteine synthase *(153,154)*. These data, showing that the lung becomes tolerant to multiple doses of naphthalene at dose levels that produced substantial toxicity in airway epithelial cells after single administration, are consistent with the 14- and 90-day oral gavage studies. This work demonstrated no significant alterations in serum enzyme levels, body weight,

Table 4.2. Species, tissue and regional differences in naphthalene toxicity

Species	Dose	Lung	
		Trachea/lobar bronchus	Terminal bronchiole
Mouse, adult, LD_{50} = 380 mg/kg	50 mg/kg	0	+
	100 mg/kg	0	++
	200 mg/kg	+/0	+++
	300 mg/kg	++	++++
	400 mg/kg	+++	++++
	11–27 mg/m^3	+/0	0
	45–61 mg/m^3	+	+/0
	133–165 mg/m^3	++	+
	383–410 mg/m^3	+++	+++
	511–591 mg/m^3	+++	+++
Mouse, adult, tolerance	200 mg/kg x 7	ND	0
	200 mg/kg x 7 + 300 (24 hours)	ND	0
	200 mg/kg x 7 + 300 (48 hours)	ND	+
	200 mg/kg x 7 + 300 (96 hours)	ND	+++
	200 mg/kg x 7 + 300 (144 hours)	ND	++++
Rat, adult, LD_{50} = 1600 mg/kg	100 mg/kg	ND	ND
	200 mg/kg	0	0
	400 mg/kg	0	0
	800 mg/kg	0	0
	1600 mg/kg	0	0
	585 mg/m^3	0	0
	0.5–1.6 mg/m^3 x 6 hours	ND	ND
	18 mg/m^3	ND	ND
	127 mg/m^3	ND	ND
Hamster, adult, LD_{50} = 800 mg/kg	200 mg/kg	0	0
	400 mg/kg	0	0
	800 mg/kg	+	0

[a] ND = not determined.

organ weight or various indices of immune function in CD-1 mice treated daily with doses up to 267 mg/kg (14 days) or 133 mg/kg (90 days) *(155)*.

Long-term exposure and carcinogenesis studies. In a subchronic study that was not published but reviewed by the European Chemicals Bureau *(22)* and evaluated in the INDEX project *(13)*, groups of 10 male and 10 female Sprague-Dawley rats were exposed snout-only to 0, 11, 51 or 306 mg/m^3 vaporized naphthalene (D. W. Coombs et al., unpublished data, 1993). Gross pathological examinations on a wide range of tissues revealed no significant changes. There were also no toxicologically relevant haematological or clinical chemistry findings. Microscopic pathology revealed treatment-related effects in the nasal passages at all

Nasal epithelium			Comments
Parenchyma	Olfactory	Respiratory	
0	0	0	No toxicity noted in liver or kidney
0	0	0	of male SW mice; ICR mice showed
0	0	0	lesions of proximal tubule at
0	ND[a]	ND	highest doses (400 and 600 mg/kg)
0	+++	0	*(136,140,147)*
0	ND	ND	West et al. *(134)*
0	ND	ND	
0	ND	ND	
0	ND	ND	
0	ND	ND	
ND	ND	ND	Areas of bronchiolar epithelial cell
ND	ND	ND	hyperplasia observed after 7 days
	ND	ND	*(150,151)*
	ND	ND	
	ND	ND	
ND	+	0	Plopper et al. *(136,140)*
0	+++	0	
0	+++	0	
0	+++	0	
0	+++	0	
0	ND	ND	
ND	+/0	0	Dodd et al. *(135)*
ND	++	0	Lee et al. *(93)*
ND	+++	0	
0	0	0	
0	+++	0	
0	+++	0	

dose levels. Degenerative changes seen in the olfactory epithelium included slight disorganization, atrophy and erosion, loss of subepithelial Bowman´s glands and signs of proliferative lesions of the olfactory epithelium. Changes were generally dose-related in that the more severe lesions and the more severe grades of all lesions occurred in the intermediate- and high-dose groups. At the lowest dose, no relevant treatment-related changes were observed in the nasal respiratory epithelium or in the lung.

Chronic exposure of B6C3F1 mice to naphthalene (53- or 160-mg/m^3) resulted in inflammation in the nose, metaplasia of the olfactory epithelium and hyperplasia of the respiratory epithelium *(156,157)*. The incidence of these lesions was 100% at both the 53- and 160-mg/m^3 exposure levels in both males and

females. The target sites for hyperplasia and metaplasia were identical to those susceptible to necrosis following acute exposures (see above). Alveolar/bronchiolar adenomas occurred in exposed male mice but the incidence did not achieve a level of statistical significance. Likewise, a small incidence of alveolar/bronchiolar carcinomas occurred in males but exposed animals did not differ statistically from unexposed. In contrast, a statistically significant though small increase in alveolar/bronchiolar adenomas was noted in high-dose (160 mg/m^3) females. Inflammation was observed in the lung of both males and females that was dose-dependent and occurred in approximately 40% of the animals in the high-dose group. There were no male/female differences in the incidence of chronic inflammation.

In similar chronic exposure studies in F 344/N rats, animals were exposed to vapour concentrations of 0, 53, 160 and 319 mg/m^3 for 105 weeks. The nasal epithelium was found to be a primary target for these exposures *(157–159)*. A dose-dependent increase in adenoma of the respiratory epithelium of the nose was noted in males, affecting 31% of the exposed population at the highest exposure levels. A much lower incidence of this lesion was observed in female rats and the incidence in exposed groups was not statistically different from that in controls. In females but not in males, there was a statistically significant increase in olfactory epithelial neuroblastomas. In several of the animals, nasal masses were observed, some of which had begun to invade the central nervous system *(159)*. A high incidence of non-neoplastic effects was observed in the nasal epithelium of both male and female rats. In the olfactory epithelium, the incidence of hyperplasia and chronic inflammation was nearly 100%, even at the lowest concentration tested (53 mg/m^3). In contrast, the respiratory epithelium was less sensitive, with 40–60% incidence for hyperplasia and inflammation in exposed animals. No differences were noted between males and females. These targets correlate well with the susceptibility of the nasal olfactory region to acute naphthalene-induced cytotoxicity and with the ability of those regions of the nasal epithelium to activate the parent substrate *(93)*.

Cataract formation. Sensitive animal models for studying naphthalene cataractogenesis have been established in rabbits *(160)*, rats *(161)* and mice *(162)*, and several in vitro methods have been used to more clearly define the mechanisms associated with the biological effects of naphthalene on the eye *(161,163)*. Doses required to produce the lesions are high: 1 g/kg per day in rabbits (number of days not specified), 1 g/kg per day for 14 days in rats and 750 mg/kg (single dose) in mice to produce a high incidence of cataracts. Van Heyningen & Pirie *(160)* presented evidence for the formation of 1,2-naphthoquinone and its involvement in cataract formation. The 1,2-quinone was thought to arise from metabolism of the parent hydrocarbon in the liver, with further processing of metabolites in the eye. Later work in mice *(162)* appears to implicate either the 1,2- or the 1,4-naph-

thoquinone. This conclusion is supported by the finding that (*a*) trichloropropylene oxide, an epoxide hydrolase inhibitor, does not alter the incidence of cataract formation and (*b*) 1-naphthol is intermediate in potency between naphthalene and the naphthoquinones, which are equipotent. Studies in rat lens cultures showed that 1,2-dihydroxy-1,2-dihydronaphthalene produced lesions similar to those observed when naphthalene was given to rats in vivo. This observation, along with the finding that an aldose reductase inhibitor blocked the lens opacity induced by the dihydrodiol, supports the importance of 1,2-naphthoquinone in mediating cataractogenesis in rats.

As indicated above, the doses used to produce cataracts in animal models are high. Lower doses, such as those reported in the subchronic oral naphthalene studies in mice (as high as 267 mg/kg per day for 14 days or 133 mg/kg per day for 90 days) apparently did not result in untoward effects in the eye *(155)*. Likewise, the chronic inhalation cancer bioassays in mice or rats did not report lesions in the eye *(123,164)*. Overall, whether these finding are relevant to humans is uncertain, since there are no reliable data on cataract formation in humans following naphthalene exposure.

Haemolytic anaemia. This principal toxicological effect of naphthalene observed in humans has not been seen in experimental animal studies with rats, mice or rabbits. The reason for this is not known. Therefore, for this end-point, there are no relevant data for extrapolation from experimental animal studies to human exposure.

Animal cells/explants/perfused tissues in vitro

As discussed in the kinetics and metabolism module, naphthalene is metabolized to several reactive metabolites that have the potential to produce the toxicities associated with the parent compound and, as discussed above, these metabolites can produce cellular injury to human cells in vitro. It is clear that naphthalene requires metabolism by the cytochrome P450 monooxygenases for lung toxicity *(84)* and that glutathione plays a major role in protecting the cells from injury *(85,165)*. There is some evidence that metabolites generated in the liver can enter the bloodstream, causing downstream toxicities in extrahepatic tissues either directly or through depletion of glutathione, with increased susceptibilities to metabolites generated in situ in the respiratory system *(108,166)*. Studies in isolated murine Clara cells *(167)* and in isolated perfused murine lung *(62,168)* demonstrated that target tissues were capable of generating sufficient metabolite from the parent compound to produce cytotoxicity in the airway epithelium. When tested in isolated Clara cells, naphthalene oxide and 1,4-naphthoquinone produced similar losses in cell viability at both 2 and 4 hours. The remaining metabolites were either less potent or did not cause a loss of cellular integrity (1-naphthol or dihydrodiol) at either point in time. Interestingly, preincubation

of cells with the cytochrome P450 monooxygenase inhibitor piperonyl butoxide inhibited the cytotoxic effects of naphthalene but not of naphthalene oxide *(167)*, a finding that suggests that metabolites downstream of the epoxide may not be keys to naphthalene toxicity. Likewise, naphthalene oxide produced selective injury to Clara cells in perfused lungs and the 1,2- and 1,4-quinones were approximately 10-fold less potent *(62)*. These studies need to be interpreted with caution, because isolated cells may or may not be a good model for the Clara cell in its normal microenvironment within the airway. Similarly, the toxicity of various metabolites in isolated perfused lungs would be strongly influenced by the amounts of these reaching the target cell from the perfusate, and there is no indication that the amounts of these were the same for the metabolites tested.

Short-term mutagenicity assays. Naphthalene and a number of naphthalene metabolites have been tested in a variety of mutagenicity assays. These have been reviewed thoroughly by IARC *(115)* and Schreiner *(169)* and will be addressed only briefly here. In all of the Ames assays using various *Salmonella typhimurium* strains, with and without activating enzyme, naphthalene is negative. As stated above, both 1,2- and 1,4-naphthoquinone were found to be positive in SCE assay *(131)*. Other short-term tests evaluating neoplastic transformations with γ-glutamyltranspeptidase-positive liver foci and in vitro cell transformation assays were, likewise, negative. Micronucleus assays for chromosome breakage were positive, as were assessments of chromosome aberrations in Chinese hamster ovary cells. Overall, the preponderance of evidence suggests that naphthalene is not a genotoxic carcinogen and that any DNA damage associated with the compound may derive from the cytotoxic actions of the naphthalene metabolites *(170)*.

The cytotoxicity associated with naphthalene exposure may play an important role in the overall effects observed in the chronic bioassay. 1,2-Naphthoquinone has been shown to bind to DNA, forming adducts at the N3 position of adenine and the N7 position of guanine that depurinate *(82)*. Recent work has disclosed formation of depurinating DNA adducts following a four-hour dermal exposure of female SENCAR mice to naphthalene, 1-naphthol, 1,2-DDN, 1,2-DHN or 1,2-NQ *(171)*. The relevance of these data is unknown, since markers of DNA reactivity associated with naphthalene in target tissues of animals and of biomarkers for evaluating these processes in humans have still to be developed *(172)*.

Health risk evaluation

Critical health outcomes

The principal health concerns of exposure to naphthalene are respiratory tract lesions, including respiratory tract carcinogenicity demonstrated in animal studies and haemolytic anaemia in humans. Regarding cataract formation seen in experimental animals after high oral exposure to (but not after inhalation of)

naphthalene, there is only suggestive evidence of an association with exposure to naphthalene in humans, if at all.

Most of the reports on haemolytic anaemia in humans refer to dermal uptake of naphthalene from clothes treated with naphthalene mothballs or unintentional or suicidal ingestion of mothballs. Many of the cases were in infants. For this end-point, data on dose–response relationships are insufficient. Since experimental rodents or rabbits do not disclose haemolytic anaemia following exposure to naphthalene, there is no relevant information from animals to extrapolate to human exposures for this effect.

No reliable data in humans are available for long-term inhalation toxicity of naphthalene, and evaluation of the risk to health of inhaled naphthalene has to rely essentially on animal studies and in vitro results. Evidence is sufficient to infer that naphthalene is a respiratory toxicant in rats and mice following acute and chronic exposure to rather low concentrations. Epithelial cells in the proximal airways are the primary target cells for naphthalene toxicity. In rats, a pronounced susceptibility of the olfactory region of the nasal mucosa was confined to the high air flow area of the medial meatus *(50)*. With increasing naphthalene concentrations, the proximal airway lesions became more severe and proceeded to the distal airways.

In two rat strains, olfactory epithelium necrosis occurred at a single six-hour whole-body exposure to the lowest naphthalene concentration of 5 mg/m^3. In a recent brief communication by Dodd et al. *(135)*, exposure to 0.5–2 mg/m^3 revealed very weak effects in a few animals, indicating a NOAEL for acute inhalation exposure. In mice, Clara cell injury was seen following a four-hour exposure to 11 mg/m^3 *(134)*.

In two reports that were not peer reviewed but have been examined and found to be of good quality, mild lesions of the nasal olfactory epithelium with signs of proliferative repair were observed following subacute or subchronic exposure down to 5 or 11 mg/m^3, respectively. This was the LOAEL after subacute or subchronic inhalation exposure (D. W. Coombs et al., unpublished data, 1993).

Compared to the acute (some hours), subacute (4 weeks) or subchronic (13 weeks) exposure studies, long-term (104 weeks) inhalation studies were performed only with relatively high naphthalene concentrations *(164)*. Chronic exposure of mice to naphthalene at 53 or 159 mg/m^3 resulted in nasal inflammation, metaplasia of the olfactory epithelium and hyperplasia of the respiratory epithelium in almost all exposed male and female animals. Alveolar/bronchiolar adenomas were seen in both exposed males and females. A statistical significance of an elevated incidence of adenomas was achieved only in the female high-dose group. A small, statistically insignificant incidence of alveolar/bronchiolar carcinomas occurred in male mice. The LOAEL for chronic respiratory tract inflammation seen with almost all mice in this study was 53 mg/m^3.

Similar chronic inhalation studies were performed in rats exposed to naphthalene at 53, 159 or 318 mg/m^3 *(123)*. In the nasal olfactory epithelium, hyperplasia, chronic inflammation and hyaline degeneration were seen in almost all animals, even in the lowest-dose group. A statistically significant dose-dependent increase in olfactory epithelial neuroblastomas occurred in females. The nasal respiratory epithelium was less sensitive, about half of the cells showing signs of hyperplasia, inflammation and hyalinization in both exposed males and females. The incidence of nasal respiratory adenomas increased dose-dependently in male rats. Again, the LOAEL for severe lesions in the olfactory region and, less pronounced, respiratory epithelium of rats chronically exposed to naphthalene was 53 mg/m^3.

The mechanisms responsible for the toxicity and carcinogenicity of naphthalene in the rodent respiratory tract and the gender differences in these responses are not fully understood. Target site cytotoxicity associated with naphthalene exposure is assumed to play a crucial role in the development of tumours observed in the inhalation studies. Studies indicate that metabolism is necessary for naphthalene to develop its cytotoxic effects. In rats, naphthalene metabolism rates are approximately 40-fold higher in the olfactory than in the septal non-olfactory mucosa *(93)*. The neuroblastomas observed in the rat olfactory epithelium are highly malignant and should be considered of relevance to humans, since P450 isoenzymes able to metabolically activate naphthalene in the rodent nose are also present in humans.

In mice, the particular susceptibility to naphthalene injury of Clara cells of the distal bronchiolar epithelium does not seem of high relevance to humans owing to the special nature of metabolism in mice *(173)*.

The possible involvement of a genotoxic mechanism in tumour formation in rodents cannot be ruled out owing to the metabolic activation of naphthalene to an epoxide, which may also be generated in the olfactory and respiratory epithelia of the rodent respiratory tract. There have been positive results in some in vitro tests for mutagenicity, but results of in vivo tests are consistently negative *(115)*. Although depurinating naphthalene-DNA adducts were identified in mouse skin *(171)*, naphthalene is not carcinogenic in this tissue.

Overall, naphthalene is considered a non-genotoxic carcinogen in the rodent respiratory tract, chronic inflammation (eventually resulting in secondary genotoxicity) being the key action in the formation of tumours.

Health relevance of indoor exposure

Indoor air levels of naphthalene may exceed outdoor concentrations manyfold owing to a variety of potential indoor sources, including tobacco smoke, indoor combustion and consumer products. Indoor air levels vary from a few to tens of μg/m^3, with levels markedly higher when mothballs are used.

Conclusions of other reviews

Naphthalene has been classified by IARC in Group 2B as "possibly carcinogenic to humans" on the basis of sufficient evidence of its carcinogenicity in experimental animals and inadequate evidence of carcinogenicity in humans *(115)*. The classification of naphthalene into carcinogenicity group Carc. 2 by the EU *(174)* and into group C by the USEPA *(16)* are compatible with the IARC evaluation.

Guidelines

The principal health concerns of exposure to naphthalene are respiratory tract lesions, including tumours in the upper respiratory tract demonstrated in animal studies and haemolytic anaemia in humans.

Lesions in the nasal olfactory and, at higher concentrations, also in the respiratory epithelia of rats appear to be the critical non-neoplastic effect. At concentrations about 100-fold higher than the lowest lesion level, severe inflammation and tumours have been reported to occur at these sites.

Increased cell proliferation due to cytotoxicity (cell damage) is considered a key element in the development of airway tumours. The likely involvement of cytotoxic metabolites in the carcinogenic response and the apparent primary non-genotoxicity of naphthalene favour the assumption of the existence of a threshold. Therefore, the use of a LOAEL/NOAEL as a threshold, combined with safety factors, is considered to be an appropriate approach for setting indoor air guidelines to minimize the carcinogenic risk to the respiratory tract of naphthalene exposure.

Associated with repeated inhalation exposure of 6 hours/day, 5 days a week for 104 weeks, severe effects in terms of inflammation were observed in almost all rats exposed to the lowest, but still relatively high, naphthalene dose of 53 mg/m^3 *(123)*. In the absence of adequately published data in relation to less severe effects, this can be taken as a LOAEL, even though it is related to severe effects.

Taking this LOAEL as a starting point and adjusting for continuous exposure (dividing by a factor of 24/6 and 7/5), a value of about 10 mg/m^3 is obtained. Further, incorporating a factor of 10 for using a LOAEL rather than a NOAEL, a factor of 10 for interspecies variation and a factor of 10 for inter-individual variation, a guideline value of 0.01 mg/m^3 is established. This guideline value should be applied as an annual average.

Extensive use or misuse of naphthalene mothballs may lead to haemolytic anaemia. Knowledge of the impact of exposure to naphthalene on the risk of haemolytic anaemia in susceptible individuals (glucose 6-phosphate dehydrogenase deficiency) cannot be used to define a guideline owing to the lack of adequate exposure data.

In the absence of mothballs or other sources such as combustion of biomass, indoor air concentrations of naphthalene are just above the typical limit of detec-

tion of about 0.001 mg/m^3. Since the concentration of naphthalene in the residential environment increases up to 100-fold when mothballs are used, the most efficient way to prevent high exposures would be to abandon (ban) the use of naphthalene-containing mothballs.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome for guideline definition

Respiratory tract lesions leading to inflammation and malignancy in animal studies.

Source of exposure–effect evidence

Nasal inflammation and olfactory epithelial metaplasia in nearly all rats chronically exposed to 53 mg/m^3 was considered as the LOAEL, even though related to severe effects *(157–159)*. This was adjusted for continuous exposure (dividing by a factor of 24/6 and 7/5). Further, a factor of 10 for using a LOAEL instead of a NOAEL, a factor of 10 for interspecies variation and a factor of 10 for inter-individual variation were incorporated, leading to a guideline value of 0.01 mg/m^3.

Supporting evidence

- Dose-dependent respiratory tract cytotoxicity following acute to chronic exposure in rats *(123)*.
- Airway toxicity was seen in several strains of rats and mice over a wide range of concentrations *(93,134–146,148,156,157)*.
- Human cells are susceptible to naphthalene metabolites in vitro *(69,131–133)*.

Results of other reviews

- IARC: Group 2B (possibly carcinogenic to humans) *(115)*.
- EU: Group 2 (suspected human carcinogen) *(174)*.
- USEPA: Group C (possible human carcinogen) *(16)*.
- EC INDEX project: guideline 0.01 mg/m^3 (annual average concentration) *(12,13)*.

Guidelines

0.01 mg/m^3 (annual average concentration).

Comments

The long-term guideline is also assumed to prevent potential malignant effects in the airways. No reliable human data for long-term inhalation toxicity are available.

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5. Nitrogen dioxide

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General description

There are seven oxides of nitrogen that may be found in the ambient air. Nitrous oxide (N_2O) is a greenhouse gas with significant anthropogenic sources contributing to its worldwide abundance (~ 0.3 ppm). However, nitric oxide (NO) and nitrogen dioxide (NO_2) are the two principal nitrogen oxides associated with combustion sources. Ambient concentrations of these two gases vary widely according to local sources and sinks, but can exceed a total concentration (NO + NO_2) of 500 μg/m^3 in dense urban areas. Nitrous acid (HONO) is a common pollutant in ambient and indoor environments, produced by the reaction of nitrogen dioxide with water.

Nitric oxide is oxidized in air to form nitrogen dioxide. In its liquid form, nitrogen dioxide is colourless to brown. While the boiling point of nitrogen dioxide is 21.15 °C, in normal ambient conditions its low partial pressure in the atmosphere (908 mmHg at 25 °C) prevents condensation so that it exists in the air in its gaseous form. In that form, nitrogen dioxide is volatile, reddish-brown in colour and heavier than air, and has a characteristic pungent odour perceptible from a concentration of 188 μg/m^3 (0.1 ppm). It is a strong oxidant, corrosive and poorly soluble in water *(1)*. Its molecular weight is 46.01 g/mol, melting point –11.2 °C, boiling point 21.15 °C and density 1.59 (air = 1). It reacts with water and is soluble in sulfuric and nitric acids.

Conversion factors

At 760 mmHg and 20 °C, 1 ppm = 1.914 mg/m^3 and 1 mg/m^3 = 0.523 ppm; at 25 °C, 1 ppm = 1.882 mg/m^3 and 1 mg/m^3 = 0.531 ppm.

Sources and pathways of exposure

In ambient air, the oxides of nitrogen are formed by various combinations of oxygen and nitrogen at high temperatures during the combustion process. The higher the combustion temperature, the more nitric oxide is generated. Indeed, 90–95% of the nitrogen oxides are usually emitted as nitric oxide and only 5–10% as nitrogen dioxide, although substantial variations from one source type to another have been observed. In ambient conditions, nitric oxide is rapidly oxidized in air to form nitrogen dioxide by available oxidants (such as oxygen, ozone and

VOCs) and this rapid oxidation velocity is such that it is nitrogen dioxide that is usually considered as a primary pollutant. In indoor air, however, this oxidation process is generally much slower *(2)*.

Road traffic is the principal outdoor source of nitrogen dioxide. The most important indoor sources include tobacco smoke and gas-, wood-, oil-, kerosene- and coal-burning appliances such as stoves, ovens, space and water heaters and fireplaces, particularly unflued or poorly maintained appliances. Outdoor nitrogen dioxide from natural and anthropogenic sources also influences indoor levels. Occupational exposures can be elevated in indoor spaces, including accidents with silage and in ice arenas with diesel- or propane-fuelled ice resurfacing machines *(3)* and underground parking garages *(4)*.

In ambient conditions, both outdoors and indoors, nitrogen dioxide exists in its gaseous form, and inhalation is therefore the major route of exposure at room temperature. Exceptionally, direct contact with the eyes and associated membranes may lead to eye irritation, although this is more likely to occur in industrial settings after accidental contact with relatively high gaseous nitrogen dioxide concentrations *(1)*.

Indoor levels and relationship with outdoor levels

Indoor air levels in various countries

In the INDEX report *(5)*, nitrogen dioxide concentrations were in the range of 13–62 μg/m^3 indoors, 27–36 μg/m^3 at the workplace, 24–61 μg/m^3 outdoors and 25–43 μg/m^3 for personal exposure. Maximum levels associated with the use of gas appliances (gas cooking and heating) in European homes are in the range 180–2500 μg/m^3. In studies regrouped in the THADE project *(6)*, mean indoor concentrations in Europe ranged from 10–15 μg/m^3 in Scandinavia *(7,8)* to 65 μg/m^3 in Poland *(8)*. Compared to European levels, indoor levels were similar in North America *(8)* but were higher in Asia (43–81 μg/m^3) *(8–10)*, New Mexico, USA *(11)* and Mexico *(8)*.

Levy et al. *(8)* studied nitrogen dioxide concentrations in homes in 18 cities in 15 countries, reporting two-day means ranging from 10 μg/m^3 to 81 μg/m^3 and personal exposures from 21 μg/m^3 to 97 μg/m^3. The use of a gas stove was found to be the dominant activity influencing indoor concentrations. Results showed also the importance of combustion space heaters to elevated nitrogen dioxide concentrations.

Numerous EU studies highlight the importance of key sources in characterizing indoor nitrogen dioxide levels. In an Italian population-based study, the highest weekly indoor concentrations were measured in a rural area of the Po Delta. The weekly mean indoor concentration in the kitchen during winter was higher than that in summer, being 62 μg/m^3 and 38 μg/m^3, respectively. The study also found that the presence of a gas-fired heating furnace was the major factor in the elevated nitrogen dioxide concentrations *(12)*. In a Spanish study of 340 dwell-

ings carried out between 1996 and 1999, average annual indoor concentrations of nitrogen dioxide did not vary significantly, ranging from 12.5 to 14.7 μg/m^3. Respective outdoor air concentrations were slightly higher in 1996 and 1998 and slightly lower in 1997 and 1999; typical indoor : outdoor ratios were close to 1. The principal indoor sources of nitrogen dioxide in Spanish homes were the use of gas cookers, the absence of an extractor fan when cooking, the absence of central heating, and cigarette smoking *(13)*. Consistent risk factors were identified when these data from Barcelona were compared with cohort data from Ashford, Kent (United Kingdom) and Menorca (Spain). In the United Kingdom, studies showed indoor concentrations of nitrogen dioxide in homes without gas stoves ranging from 13 to 40 μg/m^3 and in the presence of gas stoves from 25 to 70 μg/m^3 *(14)*.

Nitrogen dioxide concentrations in indoor air in different countries, the microenvironments and the different fuel sources are summarized in Table 5.1 (see page 268).

Factors influencing nitrogen dioxide levels indoors

Box 5.1 summarizes some of the key factors that influence indoor nitrogen dioxide levels and likely explain much of the variation reported in Table 5.1. Indoor levels of nitrogen dioxide are a function of both indoor and outdoor sources. Thus, high outdoor levels originating from local traffic or other combustion sources influence indoor levels. Annual mean concentrations in urban areas throughout the world are generally in the range of 20–90 μg/m^3 *(15)*. In the European Community Respiratory Health Survey (ECRHS II) covering 21 European cities, annual ambient nitrogen dioxide concentrations ranged from 4.9 μg/m^3 in Reykjavik to 72 μg/m^3 in Turin *(16)*. The maximum hourly mean value may be several times higher than the annual mean. For example, a range of 179–688 μg/m^3 nitrogen dioxide has been reported inside a car in a road tunnel during the rush hour *(15)*.

The distance of buildings from roadways appears to have an impact on indoor nitrogen dioxide levels *(17,18)*. Levels in school classrooms have been found to be significantly correlated with traffic density and distance of the school from the roadway *(19)*.

The air rate exchange between indoors and outdoors affects nitrogen dioxide levels in buildings. Indoor levels vary widely depending on the presence of indoor sources, air mixing within and between rooms, the characteristics and furnishing of buildings, and reactive decay on interior surfaces. Further, it has been shown that car exhausts containing nitrogen dioxide may enter a house from an attached garage *(20)*.

In the absence of indoor nitrogen dioxide sources, indoor levels will be lower than outdoor levels. Under normal ventilation conditions, the indoor : outdoor ratio has been found to vary from 0.88 to 1 *(21)*. This is attributable to the re-

Box 5.1. Factors that influence indoor concentrations of nitrogen dioxide

Indoor sources

Fuel-burning stoves (wood, kerosene, natural gas, propane, etc.)
Fuel-burning heating systems (wood, oil, natural gas, etc.)
Tobacco use

Source characteristics

Flued/unflued sources
Presence of pilot lights

Outdoor sources (via infiltration)

Mobile sources (petrol- and diesel-powered vehicles)
Stationary sources (industrial combustion)

Resident behaviour

Stove usage (for fuel-burning appliances)
Use of heating equipment (including cooking stoves)

Dwelling and indoor environment characteristics

Dwelling size (where there are indoor sources)
Air exchange rates
Distance to roadway
Surface characteristics
Indoor humidity

moval of nitrogen dioxide by the building envelope and its reactions with interior surfaces and furnishing *(22)*. However, in the presence of indoor sources, especially unvented combustion appliances, indoor levels may exceed those found outdoors *(23)* with an increase in the indoor : outdoor ratio from 0.7 without an indoor source to 1.2 in the presence of an indoor source *(3,24,25)*. These ratios, however, reflect average levels over several days of measurement and do not reflect the more extreme indoor/outdoor differences that one would expect to see over shorter periods of time – for example, when a gas appliance is being used inside a home.

The presence and use of indoor sources are the primary determinants of indoor nitrogen dioxide levels within populations. In an inner-city population in the United States, mean nitrogen dioxide concentrations were higher in homes with a gas stove (33.1 ppb or 63.3 $\mu g/m^3$) than in those without a gas stove (16.8 ppb or 32.1 $\mu g/m^3$) *(26)*. In this study, indoor levels were also associated with the presence of a gas heater and the use of a space heater or oven for supplementary heating.

The average nitrogen dioxide concentration over a period of several days may exceed 150 $\mu g/m^3$ when unvented gas stoves are used *(27)*. On the other hand, wood-burning appliances were not related to elevated nitrogen dioxide concentrations in a Canadian study carried out in 49 houses *(28)*. While most studies

of indoor air pollutant exposures from biomass burning in developing countries have focused on airborne particulate matter, nitrogen dioxide levels can also be elevated. In a study in Ethiopia where wood, crop residues and animal dung were the main household fuels, the mean 24-hour concentration of nitrogen dioxide was 97 μg/m^3 *(29)*. A study in rural, urban and roadside locations in Agra, India showed the dominance of outdoor sources (principally diesel generators and traffic) on elevated indoor nitrogen dioxide concentrations (indoors 255 ± 146 ppb; outdoors 460 ± 225 ppb) *(30)*.

Indoor levels are typically higher in winter than in summer, probably owing to increased use of heating, lower ventilation rates and higher outdoor concentrations *(11,14,31,32)*. In the recently published ECRHS II study carried out in 21 European cities, concentrations in winter exceeded summer values with an average winter : summer ratio of 1.50 *(16)*.

There are limited data on nitrogen dioxide peaks. However, it has been shown that, in homes, peak concentrations are typically related to the use of combustion appliances for cooking and heating *(32–35)*. In particular, occurrences of peaks are strongly associated with the use of gas and solid fuel stoves, the highest nitrogen dioxide concentrations coinciding with the time of meal preparation *(36)*. In a study of Australian homes, the mean peak-to-average nitrogen dioxide ratio was 2.9 (1.2–4.6) for homes without gas cookers and 7.8 (2.6–13.0) for those with gas cookers *(37)*. A modelling study of indoor nitrogen dioxide exposures in the United Kingdom concluded that those regularly using gas for cooking would experience 1-hour mean exposures above 287 μg/m^3 (150 ppb) for at least 1 hour on every day of the year *(38)*. Reported maximum measured nitrogen dioxide levels associated with the use of gas appliances in homes are in the range 150–2055 μg/m^3 over 1 hour, with peaks of 400–3808 μg/m^3 for 1 minute *(27,34)*.

In addition to the direct release of nitrogen oxides, indoor combustion sources emit various co-pollutants including ultrafine particles, which are also produced during cooking *(36)*. Secondary reactions, such as the production of nitrous acid from surface chemistry involving nitrogen dioxide, can contribute to indoor pollutant concentrations that directly affect health *(39,40)*. The role of these co-pollutants in the health effects attributed to nitrogen dioxide in field studies is unknown, but abatement measures for nitrogen dioxide, such as improved ventilation, will be beneficial in reducing co-exposures also.

High nitrogen dioxide concentrations are also associated with the use of candles and mosquito coils. In chamber (18 m^3) tests, maximum nitrogen dioxide concentrations up to 92 μg/m^3 were observed during incense burning *(41)*. High values of nitrogen dioxide up to 7530 μg/m^3 were also reported in enclosed ice arenas with inadequate ventilation from the exhaust emissions of propane- and petrol-fuelled ice resurfacing machines *(42,43)*. The link between direct source exposure and high nitrogen dioxide levels was noted in a small study of unvented natural gas fireplaces (mean 688.7 μg/m^3; n = 2) *(33)*.

Indoor concentrations of nitrogen dioxide are also subject to geographical, seasonal and diurnal variations. Differences in the indoor concentrations in various countries are mainly attributable to differences in the type of fuel used for cooking and heating and the rate of fuel consumption. While few studies have included repeated measurements of indoor nitrogen dioxide levels, it is known that within-home variability can be significant owing to the various contributing factors discussed above *(44)*.

Seasonal variability can be significant, owing to variations in source use (e.g. heaters and stoves) and seasonal fluctuations in air exchange rates. This variability results typically in higher indoor concentrations during winter months *(31,45,46)*. This variability, and its principal determinants, should be considered when extrapolating from exposure estimates determined using daily or weekly measurements to estimates of annual exposures. Since few (if any) studies have directly measured annual averages of indoor nitrogen dioxide concentrations, periodic measurements across seasons would be needed to construct representative estimates of long-term exposure.

Kinetics and metabolism – effects observed in experimental studies

In vitro studies

As nitrogen dioxide is a free radical, it has the potential to deplete tissue antioxidant defences and, as a consequence, cause injury and inflammation as shown in a variety of in vitro test systems. Exposure of human blood plasma to 26 230 $\mu g/m^3$ (13.95 ppm) nitrogen dioxide resulted in a rapid loss of ascorbic acid, uric acid and protein thiol groups, in addition to lipid peroxidation and a depletion of alpha-tocopherol (vitamin E) *(47)*.

In another study, exposure to nitrogen dioxide over a lower concentration range (94–1880 $\mu g/m^3$; 0.05–1.0 ppm) resulted in the antioxidant defences, uric acid and ascorbic acid being depleted in human bronchoalveolar lavage (BAL) fluid *(48)*. More recently, Olker et al. *(49)* have shown that superoxide radical release is significantly impaired from BAL cells isolated from rats exposed to nitrogen dioxide (18 800 $\mu g/m^3$; 10 ppm) for 1, 3 or 20 days. This was explained by decreased production as a result of an inhibition of NADPH oxidase and complex III of the respiratory chain, and to a lesser extent increased scavenging brought about by enhanced glutathione peroxidase and CuZn-superoxide dismutase mRNA expression and enzyme activities. Evidence for the role of oxidative stress in the effects of nitrogen dioxide on respiratory virus-induced injury comes from a study that found that pre-treatment of cultured primary human nasal epithelial cells and cells of the BEAS-2B line with the antioxidant *N*-acetylcysteine inhibited the production of IL-8 following exposure to 3160 $\mu g/m^3$ (2 ppm) nitrogen dioxide for three hours in combination with human rhinovirus type 16 (RV16) *(50)*.

Cell culture systems have also been used to describe nitrogen-dioxide-mediated cell injury and inflammation. One system exposed cultured human bronchial epithelial cells to 7520 and 15 040 μg/m^3 (4.0 and 8.0 ppm) nitrogen dioxide and elicited cell membrane damage and increased membrane permeability *(51)*. It should be remembered that confluent airway epithelial cell monolayers in vitro are not fully differentiated and posses a markedly decreased level of resistance to pollutants when compared to the epithelium in the intact human. However, in a more physiologically relevant system, nitrogen dioxide (200 and 800 μg/m^3; 0.1 and 0.43 ppm) has also been shown to trigger inflammation in cultured human nasal mucosa explants, using histamine release into the culture medium as a marker of the inflammatory response *(52)*. The early pro-inflammatory responses following exposure to a brief high concentration of nitrogen dioxide – up to a maximum of 84 600 μg/m^3 (45 ppm) over 50 minutes – have also been assessed using normal human bronchial epithelial (NHBE) cells as an in vitro model of inhalation injury *(53)*. While immunofluorescence studies confirmed oxidant-induced formation of 3-nitrotyrosine, the nitrogen-dioxide-exposed cells exhibited marked increases in the levels of nitrite (used as an index of nitric oxide), IL-8, IL-1β and TNF-α. Further, to simulate a pre-existing "inflammatory" condition of the bronchial epithelium, such as would exist in asthma and other hyperreactive airway diseases, cells were pre-treated with various pro-inflammatory cytokines (IFN-γ, TNF-α, IL-1β and IL-8) for 24 hours prior to exposing them to nitrogen dioxide. The combination of cytokine treatment and nitrogen dioxide exposure consistently enhanced the generation of nitric oxide and IL-8. More recently, further findings have been published on the early changes in NHBE cells on exposure to a brief high dose (84 600 μg/m^3; 45 ppm) of nitrogen dioxide, focusing on the nature and time-course of nitrogen-dioxide-mediated cell death and, more generally, on the cellular mechanisms by which the various pro-inflammatory mediators affect the target cells *(54)*. Cells were found to undergo apoptotic cell death during the early post-nitrogen-dioxide period, independent of any significant increase in caspase-3 activity, while necrotic cell death was more prevalent at later time intervals. Exposed cells also exhibited increased expression of heme oxygenase-1 (HO-1), a redox-sensitive stress protein, at 24 hours and increased adhesion to neutrophils, which in turn resulted in an increased NHBE cell death. Earlier reports of an involvement of nitric oxide *(53)* were supported by the significant decrease in cell death and neutrophil adhesion in the presence of nitric oxide synthase inhibitors (L-NAME and 3-aminoguanidine) *(54)*.

Effects on experimental animals

Nitrogen dioxide per se, but not specifically in relation to indoor sources/exposure patterns, has been shown to exert a range of biological effects on experimental animals, including changes in lung metabolism, structure, function, inflam-

mation and host defence against infectious pulmonary disease. Such effects vary widely, however, depending on the species and strain exposed, the concentration and duration applied, and the age and sex of the animals *(55)*.

In extrapolating the aforementioned data to humans, it is the anatomical and physiological differences between animals and humans that represent a particular challenge. For example, we have known for some time from mathematical modelling that the distribution of nitrogen dioxide deposition within the respiratory tract of rats, guinea-pigs, rabbits and humans appears to be similar *(56–58)*. More recently however, Tsujino et al. *(59)*, using mathematical airway models of rats, dogs and humans, demonstrated that interspecies variations in anatomy and respiratory patterns do cause significant differences in the concentration of nitrogen dioxide in the airways and alveoli. Despite some limitations, owing to many simplifications and assumptions necessary to construct the airway model and carry out calculations, intra-airway nitrogen dioxide concentrations were higher in the upper and lower airways of humans compared with rats and dogs, while those in the alveolar regions were lowest in humans.

Pulmonary metabolism

The majority of biochemical studies show effects only after acute or subchronic exposure to high levels of nitrogen dioxide exceeding 3160 μg/m^3 (2 ppm) *(60–62)*. A notable exception is the effect on lung lipid metabolism. Continuous exposure of rats to concentrations as low as 752 μg/m^3 (0.4 ppm) for 18 months increased lipid peroxidation when thiobarbituric acid reactants were used as an indicator, while lipid peroxidation was raised by 75 μg/m^3 (0.04 ppm) for 9 months when ethane exhalation was the indicator *(63,64)*. Effects on both lipid and antioxidant metabolism showed a response pattern that depends on both concentration and duration of exposure *(65)*. Frequently observed features at higher nitrogen dioxide levels include the induction of lung oedema, an increase in antioxidant metabolism, an increase in lung enzymes associated with cell injury, and changes in lung lipids. On investigating the basis of oxidative stress elicited in rats exposed to 18 880 μg/m^3 (10 ppm) nitrogen dioxide for 3 and 20 days (inducing acute and chronic lung injury, respectively), Hochscheid et al. *(66)* reported an imbalance of glutathione status (by analysing the activity and mRNA expression of a host of enzymes involved in glutathione metabolism) in type II pneumocytes following both types of lung injury.

In relation to nitrogen-dioxide-induced oxidative stress and perturbations in antioxidant metabolism, a potential protective role that antioxidant status may play in influencing the lung response to pollutant exposure has been explored *(67)*. The effects of a low-selenium diet (1.3 μg/day) with or without selenium supplementation in rats exposed to either acute (62 000 μg/m^3 (50 ppm) for 30 minutes), intermittent subacute (5 ppm, 6 hours/day for 5 days) or intermittent long-term nitrogen dioxide (1 or 10 ppm, 6 hours/day, 5 days/week for 28 days)

on a host of markers were examined and the majority of these (particularly those indicating increased permeability of the lung epithelial barrier) indicated the protective role of normal selenium status.

Although still not fully understood, alterations in pulmonary metabolism may be early signs of cell lesions, which become manifest only at higher concentrations or upon longer exposure *(60–62,68,69)*.

Pulmonary structure

In the tracheobronchial and alveolar regions, nitrogen dioxide at concentrations down to 640 μg/m^3 (0.34 ppm) results in replacement of the type I alveolar epithelial and ciliated epithelial cells with the more oxidant-resistant type II and nonciliated bronchiolar (Clara) cells, respectively. Furthermore, the replaced cells exhibit alterations of their cytoplasm and hypertrophy after short exposure (10 days) to concentrations of nitrogen dioxide above 940 μg/m^3 (0.50 ppm), the significance of which is not known (*60–62,69)*. We do, however, appreciate that both the exposure regimen used and the time of exposure are important. In a subchronic study of lung lesions in rats, Rombout et al. *(70)* showed that the concentration (C) of inhaled nitrogen dioxide had more influence on epithelial metaplasia than exposure duration (time, T) when C × T was constant, and that the effect of C was greater with intermittent exposure than with continuous exposure. Other experiments have addressed the temporal pattern of nitrogen dioxide effects and found them to be complex *(60)*. For example, over a 7-day period, a wave of epithelial hyperplasia occurs, peaking by about day 2 *(71)*. Rombout et al. *(70)* showed that even 2 months after a 1-month exposure ceased, some nitrogen-dioxide-induced interstitial changes were still present.

Long-term exposure to nitrogen dioxide leads to emphysema-like structural changes in animals, in addition to thickening of the alveolar capillary membrane, loss of ciliated epithelium and increases in lung collagen. Such changes have been observed in mice, rats, dogs and monkeys (*60–62,68)*. In 1993, the USEPA reviewed 23 research reports on nitrogen dioxide exposure and emphysema to determine whether the effects reported met the US National Heart, Lung, and Blood Institute definition for human emphysema *(72)*. This can be important because the animal studies were of interest for the purposes of extrapolation to humans, whether or not the more rigorous definition of human emphysema (which includes destruction of alveolar walls) is met. Many of the reports contained insufficient detail to permit an independent judgement as to whether "human-type" emphysema had occurred. Nevertheless, three studies reported convincing evidence of human-type emphysema following exposure to very high nitrogen dioxide levels relative to ambient concentrations: Haydon et al. *(73)* exposed rabbits to 15 040–22 600 μg/m^3 (8–12 ppm) for 3–4 months; Freeman et al. *(74)* exposed rats to 37 000 (reduced to 28 200 or 18 800) μg/m^3 (20, reduced to 15 or 10 ppm) for up to 33 months; and Hyde et al. *(75)* exposed dogs for 5½ years to a

mixture containing 1210 μg/m³ (0.64 ppm) nitrogen dioxide and 310 μg/m³ (0.25 ppm) nitric oxide, respectively. These animals exhibited several decrements in pulmonary function, which continued to deteriorate compared to controls during a 2½-year post-exposure period in clean air. After this post-exposure period, lung morphometry studies showed changes analogous to human centrilobular emphysema.

Studies undertaken to localize collagen deposition within the lung have exposed ferrets to 940 or 18 800 μg/m³ (0.5 or 10 ppm) of nitrogen dioxide for 4 hours a day for 8 or 15 weeks. Increased lung collagen deposition was identified within the respiratory bronchiolar submucosa, although this was only significant in the higher-dose group *(76)*. The onset of emphysema-like changes, together with the major features characteristic for human chronic obstructive pulmonary disease (COPD), have also been reported in another study in which mice were exposed to 31 160 μg/m³ (20 ppm) nitrogen dioxide for 14 hours a day for up to 25 days *(77)*. The main findings were progressive airway inflammation with a marked influx of neutrophils and macrophages, goblet cell hyperplasia indicative of increased mucus hypersecretion in the central airways, progressive airflow obstruction and focal parenchymal inflammation associated with airspace enlargement. Exposure of rats to 18 880 μg/m³ (10 ppm) nitrogen dioxide for 23 hours per day for 3, 7 or 21 days, or 21 days followed by 28 days in room air, resulted in increased alveolar septal cell turnover, indicated by an 8-fold increase in alveolar septal cell apoptosis at day 3 and a 14-fold increase in proliferation *(78)*. These changes led to accelerated lung growth, characterized by an imbalance in the relative composition of the extracellular matrix, but failed to induce emphysema. Indeed, although airspace enlargement was evident, nitrogen dioxide resulted in an increase in the total surface area and absolute volume of alveolar walls comprising all compartments.

Pulmonary function

Exposure to nitrogen dioxide at concentrations of 376–18 800 μg/m³ (0.2–10 ppm) has been shown to affect pulmonary function in several animal species (rats, mice, guinea-pigs and ferrets). The extent of an effect may be influenced by the mode of exposure, in that compared to continuous exposure (376 μg/m³; 0.2 ppm) alone, a greater reduction in end-expiratory volume, vital capacity and respiratory system compliance was shown in mice chronically exposed to 1-hour spikes (twice a day) of 1504 μg/m³ (0.8 ppm) of nitrogen dioxide superimposed on the baseline exposure *(79)*. Adult rats exposed for 6 weeks to 940 μg/m³ (0.5 ppm) nitrogen dioxide and daily 1-hour spikes of 2820 μg/m³ (1.5 ppm) experienced reduced lung compliance that returned to normal 3 weeks post-exposure *(80)*. An increase in lung volume and compliance was seen (at 3 weeks but not at 6 weeks) in neonatal rats exposed to an identical regimen *(80)*. A chronic (78-week) exposure study assessed a number of pulmonary function parameters in

rats exposed to nitrogen dioxide (940 μg/m^3 (0.5 ppm) background with a daily peak rising to 2820 μg/m^3 (1.5 ppm)). No changes in compliance, lung volume or diffusion capacity of carbon monoxide were seen, while a decrease in the delta forced expiratory flow at 25% of forced vital capacity disappeared soon after the end of exposure *(81)*. In guinea-pigs exposed to 112.8, 940 or 1880 μg/m^3 (0.06, 0.5 or 1.0 ppm) nitrogen dioxide for 6 or 12 weeks, significant effects were limited to an increase in pulmonary specific airway resistance in 13% (2 of 15) of animals following the 12-week 1.0-ppm exposure regimen *(82)*. The effect of exposure to either 940 or 18 800 μg/m^3 (0.5 or 10 ppm) nitrogen dioxide on tracer particle clearance from the airways of ferrets during postnatal respiratory tract development has also been examined. Thoracic clearance was reduced in both exposure groups, but was not significantly different in the 940-μg/m^3 (0.5-ppm) group compared to that of the control animals exposed to clean air *(76)*.

Airway inflammation and responsiveness

The effects of short-term (24-hour) exposure to nitrogen dioxide on airway eosinophilic inflammation and bronchial hyperreactivity have been examined using a standard murine model of antigen-modified broncho-constriction and airway inflammation *(83)*. BALB/c mice were sensitized to ovalbumin and exposed to 3760 μg/m^3 (2.0 ppm) nitrogen dioxide prior to being challenged with aerosolized ovalbumin on days 13 and 14. Nitrogen dioxide was found to enhance epithelial damage, reduce mucin expression and increase baseline smooth muscle tone. Although a modest increase in airway neutrophilia was detected, exposure was not associated with airway eosinophilia or with an increase in bronchial hyperresponsiveness. In contrast, Poynter et al. *(84)* reported no changes in the inflammatory response in C57BL/6 mice immunized and challenged with ovalbumin before exposure to 3 days of 9400 μg/m^3 (5 ppm) nitrogen dioxide. A 5-day inhalation of 31 000 μg/m^3 (25 ppm) nitrogen dioxide was, however, found to prolong ovalbumin-induced inflammation and airway hyperresponsiveness. Findings included acute damage associated with inflammation and lesions in the alveolar duct region and an influx of macrophages and neutrophils into the lavageable air spaces. Moreover, 20 days after cessation of the inhalation regimen, eosinophilic and neutrophilic inflammation, pulmonary lesions and airway hyperresponsiveness were still present.

A hypothesis that nitrogen dioxide acts as an effective inhaled adjuvant that accentuates the adaptive immune response to otherwise innocuous antigens prompted a study in which mice were exposed first to 18 880 μg/m^3 (10 ppm) nitrogen dioxide and then to aerosolized 1% ovalbumin *(85)*. Mice were subjected to the same sensitization regimen one week after and challenged with 1% ovalbumin alone an additional week later. Following the final challenge with ovalbumin, mice developed eosinophilic inflammation, mucus cell metaplasia, airway hyperresponsiveness and antigen-specific IgE and IgG1, and Th2-type cytokine

responses. The authors likened these changes to the phenotypic alterations in allergic asthma and those elicited following ovalbumin challenge in antigen-sensitized mice.

The inflammatory response to nitrogen dioxide, with particular focus on the activation state of alveolar macrophages, has been studied in a rat inhalation model using continuous exposure to 18 800 μg/m^3 (10 ppm) for 1, 3 and 20 days *(86)*. Whereas the number of inflammatory cells and total protein concentration in BAL were increased, TNF-α was markedly reduced with increasing exposure time. In contrast, IL-10, IL-6 and suppressor of cytokine signalling-3 protein were elevated. Furthermore, in vitro lipopolysaccharide stimulation of BAL cells revealed reduced capability to produce TNF-α, IL-1 β and nitric oxide, but showed markedly increased transcription and protein release for IL-10. In addition, elevated levels of IL-6, scavenger receptor B and suppressor of cytokine signalling-3 mRNA were detected in BAL cells from exposed animals. Analyses of highly purified alveolar macrophages indicated that changes in the activation state of these cells were most likely responsible for the observed effects.

To increase our understanding of the contribution of nitrogen dioxide to the development of COPD, Brandsma et al. *(87)* studied the effects of combined exposure to nitrogen dioxide and cigarette smoke on pulmonary inflammation and emphysema. Mice were exposed to either 31 160 μg/m^3 (20 ppm) nitrogen dioxide for 17 hours a day, 24 puffs of cigarette smoke twice a day or both, 5 days a week for 4 weeks. Cigarette smoke exposure increased eosinophil numbers and levels of TNF-*α*, KC (mouse IL-8), monocyte chemoattractant protein (MCP)-1, and IL-6. Nitrogen dioxide exposure increased goblet cells, eosinophils and the levels of IL-6, while it reduced the levels of IL-10. Four weeks of nitrogen dioxide, cigarette smoke or both was not sufficient to induce significant emphysema, nor did it lead to lower numbers of lymphocytes, neutrophils or macrophages in lung tissue. Instead, nitrogen dioxide exposure dampened the cigarette smoke-induced increases in the inflammatory cytokines TNF-*α*, KC and MCP-1. The authors suggested that these attenuating effects may be due to modulating effects of nitrogen dioxide on cytokine production by macrophages and epithelial cells. Clearly, cigarette smoke contains a range of radical species, including nitrogen dioxide, and these data may simply reflect the induction of similar pathways by both challenges.

Host defence

Several types of animal study have indicated that nitrogen dioxide increases susceptibility to respiratory infections *(60,61,88–90)*. An extensive set of data was collected using the infectivity model, which measures the total antibacterial defences of the lungs of mice. For long-term exposures, the lowest concentration tested that increased mortality when challenged with *Klebsiella pneumoniae* was 940 μg/m^3 (0.5 ppm) for 3 months of exposure *(91)*. After a 3-hour exposure, the

lowest concentration tested that affected resistance to *Streptococcus pneumoniae* was 3760 μg/m^3 (2 ppm) *(92)*. Continuous exposure to concentrations ranging from 52 640 to 940 μg/m^3 (from 28 to 0.5 ppm) resulted in linear, concentration-related increases in mortality due to pulmonary infection *(93)*. Other studies have shown that peak and patterns of nitrogen dioxide exposure are important in determining response *(60,79,94)*. For example, Miller et al. *(79)* found that infectivity, mortality and pulmonary function deficits in mice were significantly greater following a spiked exposure regimen (up to 52 weeks of continuous baseline 376 μg/m^3 (0.2 ppm) plus spikes of 1504 μg/m^3 (0.8 ppm) compared to the baseline exposure alone). In mice exposed to nitrogen dioxide at 8460 μg/m^3 (4.5 ppm) for 1, 3½ or 7 hours and challenged with *Streptococcus* sp. either immediately or 18 hours after exposure, the mortality rate was directly related to the length of peak exposure when the streptococcal challenges were immediately after nitrogen dioxide exposure but this was not the case when the challenge was delayed for 18 hours *(94)*. In summary, the body of work shows that the effects of nitrogen dioxide are due more to concentration than to duration of exposure or to total dose (expressed as C × T), that differences in species sensitivity exist, that the lowest effective concentration of nitrogen dioxide also depends on the microbe used in the test, and that low levels only cause effects after repeated exposures *(60–62,68)*. The extrapolation of these findings to humans cannot be made directly, because most of the studies used pneumonia-induced mortality as an end-point. However, the infectivity model reflects alterations in the defence mechanisms of mice that are shared by humans. Nevertheless, the quantitative relationship between effective nitrogen dioxide levels in animals and in humans is unknown. Although numerous studies provide evidence of the effects on the systemic humoral and cell-mediated immune systems, these studies are difficult to interpret *(60,61)*.

In mice, an exposure of 9400 μg/m^3 (5 ppm) nitrogen dioxide (following the bacterial challenge) was required to impair the intrapulmonary killing of *Staphylococcus aureus (90)*. The same effect, however, was found at 3100 μg/m^3 (2.5 ppm) or less in lungs immunosuppressed with corticosteroids, while the adverse effect of the pollutant was only evident at 18 800 μg/m^3 (10 ppm) when exposure preceded the bacterial challenge *(90)*.

The association between exposure to common air pollutants, including nitrogen dioxide, and altered host immunity to respiratory viral infections has recently been reviewed *(95)*. Two studies by Rose et al. *(88,89)* exposed mice to nitrogen dioxide at 9400 μg/m^3 (5 ppm) for six hours per day for two days prior to infection with murine cytomegalovirus, followed by another four days of nitrogen dioxide. The mice exposed to nitrogen dioxide not only required 100-fold less virus to become infected (possibly due to reduced phagocytosis and macrophage destruction of the virus in the pollutant-exposed mice) but were more likely to be re-infected with murine cytomegalovirus, suggesting that exposure

can adversely affect the development of virus-specific immunity. Enhanced susceptibility to infection was not found after exposure to 3100 or 1800 μg/m^3 (2.5 or 1 ppm) nitrogen dioxide. In another study using mice and the Sendai virus, while exposure to 9400 μg/m^3 (5 ppm) nitrogen dioxide for four hours per day did not alter infection it did enhance lung damage, which was suggested to have been caused by increased proliferation of the virus *(90)*.

Mutagenic/genotoxic/carcinogenic effects

There are no reports among the limited number of carcinogenicity studies that nitrogen dioxide causes malignant tumours or teratogenesis *(60,61,96,97)*. High (11 280–28 200 μg/m^3; 6–15 ppm) concentrations of nitrogen dioxide have been shown to be mutagenic in bacterial (*S. typhimurium*) test systems *(98)*. In vitro genotoxicity studies have reported chromosomal aberrations, sister chromatid exchanges or DNA single strand breaks at concentrations ranging from as high as 31 160 μg/m^3 (20 ppm) to as low as slightly over 1800 μg/m^3 (1 ppm) but not 940 μg/m^3 (0.5 ppm) *(99–101)*. Genotoxicity studies in vivo have produced mixed results. While lung cells of rats exposed to nitrogen dioxide for three hours exhibited increased mutation to ouabain resistance at 28 200 μg/m^3 (15 ppm) and increased chromosome aberrations at 15 040 μg/m^3 (8 ppm) *(102)*, no genotoxic effects were reported in alveolar macrophages of rats exposed to 2256 μg/m^3 (1.2 ppm) for three days *(103)*, in bone marrow after inhalation by mice of 31 160 μg/m^3 (20 ppm) for 23 hours *(104)* and in spermatocytes or lymphocytes of mice following a six-hour exposure to 180–18 000 μg/m^3 (0.1–10 ppm) *(105)*. Numerous studies of the interaction of nitrogen dioxide with other air pollutants, predominantly ozone, show that the effects are due to ozone alone, are additive or are synergistic, depending on the end-point and exposure regimen *(60)*.

Reproductive effects

A recent study has examined effects in the rat of fetal exposure to diesel-engine exhaust containing nitrogen dioxide at 1504 or 188 μg/m^3 (0.80 or 0.10 ppm) with or without particulate matter (1.71 or 0.17 mg/m^3) on testicular cell numbers and daily sperm production in adulthood *(106)*. The mature rats that were exposed to diesel exhaust from gestational day 7 to delivery showed a decrease in the daily production of sperm due to an insufficient number of Sertoli cells. All exhaust-exposed groups showed almost the same reactions to the inhalation, indicating that the gaseous phase must have included the responsible toxicants; these were not identified, although nitrogen dioxide would be a major constituent.

Experimental studies – summary

Experimental animal work on the health effects, and mechanisms thereof, of nitrogen dioxide has not focused on indoor sources or exposure patterns

of the pollutant (other, of course, than to have conducted all studies in an indoor environment). As such, in addition to newly published work, the studies reviewed in this section include those described in WHO's latest guidelines for ambient nitrogen dioxide *(15)*. Acute exposures (hours) to low (75–1880 μg/m^3; 0.04–1.0 ppm) levels of nitrogen dioxide have rarely been observed to cause effects in animals. Subchronic and chronic exposures (weeks to months) to low levels, however, cause a variety of effects, including alterations to lung metabolism, structure and function, inflammation and increased susceptibility to pulmonary infections. Emphysema-like changes (destruction of alveolar walls and airspace enlargement), features characteristic of human COPD (increased mucus production and progressive airway obstruction), generation of an atopic immune response and airway hyperresponsiveness have been reported only at high (15 040–47 000 μg/m^3; 8–25 ppm) nitrogen dioxide concentrations. It is apparent from both in vitro and animal toxicology studies which toxic effects of nitrogen dioxide *might* occur in humans. Nevertheless, owing to (*a*) the frequent use of extremely high exposure concentrations in experimental studies, (*b*) the inherent differences between mammalian species and (*c*) the dearth of information available on tissue response of different species to a given dose of nitrogen dioxide, it is difficult to extrapolate quantitatively, with any degree of confidence, the effects that are *actually* caused by a specific inhaled dose or concentration.

An important point, worthy of consideration, is the possible interaction between nitrogen dioxide and other indoor pollutants. It is increasingly acknowledged by indoor environmental scientists that it is the reactions between primary pollutants, creating secondary pollutants indoors, that are probably responsible for adverse health effects.

Health effects

A plethora of outdoor studies have examined the health effects of exposure to outdoor nitrogen dioxide. While there are concerns that some of the associations reported for health effects and outdoor nitrogen dioxide may be explained by co-pollutants, extensive reviews have concluded that respiratory health is associated with nitrogen dioxide exposure, independently of these other exposures *(15,107)*.

Outdoor nitrogen dioxide is increasingly being implicated in a wide range of disorders. For example, increased risk of otitis media *(108)*, eczema *(109)* ear/nose/throat infections and sensitization to food allergens *(110)* in children, as well as increased blood coagulability after periods of elevated ambient exposure in adults *(111)* have recently been reported. There is also an increasing interest in the role of outdoor pollution with reproductive outcomes *(112)*. A full review of these is beyond the scope of this report. This section will:

- briefly summarize conclusions from earlier WHO reports on the evidence for health effects based on controlled human exposure studies;

- review the epidemiological evidence for health effects of exposure to indoor nitrogen dioxide where nitrogen dioxide has been directly measured; and
- review the epidemiological evidence for health effects of exposure to gas appliances in the home – a proxy marker for high exposure to indoor nitrogen dioxide.

Controlled human clinical studies

Studies in which exposure to nitrogen dioxide has been carefully controlled in small numbers of selected participants have been reviewed in several previous publications *(15,62,107)*. These studies have examined symptoms, changes in pulmonary function and changes in airway reactivity in healthy volunteers and in those with pre-existing lung disease. Some studies have included bronchoalveolar lavage following exposure and have provided information on the inflammatory changes that may occur.

There are some inconsistencies in the results of these studies but studies on healthy volunteers can be summarized as follows.

- Measurable change in lung resistance, total airway resistance and bronchial responsiveness to acetylcholine and methacholine in healthy volunteers has been seen at exposures in excess of 1880 μg/m^3, although in one study exposures well in excess of this (7520 μg/m^3 for 75 minutes) failed to show any change *(113)*.
- A study in which nitrogen dioxide exposure was followed by bronchoalveolar lavage with assessment of cell profile in lavage fluid and in blood suggested that high exposure (up to 2821 μg/m^3 for three hours) is associated with mild airway inflammation, changes in white blood cells and increased susceptibility of airway epithelial cells to injury from respiratory virus (as assessed in vitro) *(114)*. Two studies (one at 2821 μg/m^3, the other at 7524 μg/m^3 and both for 20 minutes on 6 occasions) found decreased alveolar macrophages and lymphocyte subgroups in bronchoalveolar lavage fluid *(115,116)*. Repeated exposure to 1128 μg/m^3 for two hours on four days did not change the percentage of neutrophils, total lymphocytes or macrophages in blood and lavage fluid, although small increases in the percentage of killer cells in lavage fluid were observed *(117)*. Repeated exposure for four hours to 3760 μg/m^3 daily for four days *(118)* and for four hours to 3760 μg/m^{3}daily for three days *(119)* was associated with evidence of neutrophilic inflammation. Similar patterns of exposure in healthy volunteers have been associated with increased expression of IL-5, IL-10 and IL-13 in bronchial biopsies, suggesting an upregulation of TH2 cytokines consistent with a pro-allergic effect *(120)*, even when pulmonary function changes are not observed. These authors also observed an increase in expression of ICAM-1, which may indicate a mechanism by which nitrogen dioxide exposure could be associated with increased respiratory infections.

- Exposure to nitrogen dioxide at levels of 3600 μg/m^3 in healthy subjects produced changes in bronchoalveolar lavage fluid consistent with oxidative stress (low levels of uric acid and ascorbate), with evidence of a relatively short-lived (< 24-hour) protective response in the form of increased glutathione levels *(121)*. The initial loss of antioxidants in bronchoalveolar lavage fluid may be attenuated with repeated exposures *(118)*.
- Repeated exposures above 1880 μg/m^3 for two hours per day over three days may be associated with increased susceptibility to infection with influenza virus *(122)*. A three-hour exposure to 1128 μg/m^3 may be sufficient to inhibit the alveolar macrophage response to the influenza virus *(123)*.

Results from controlled exposure to nitrogen dioxide in those with pre-existing lung disease can be summarized as follows.

- People with asthma exposed to 560 μg/m^3 for up to 2.5 hours may experience relatively minor changes in pulmonary function *(124–126)* but this is by no means consistent across studies. Studies with much higher exposures have failed to show any effect *(127)* and some studies showing small effects at lower exposures have been difficult to reproduce *(128)*. Similar inconsistencies have been observed when people with COPD have been studied.
- Two meta-analyses of the association of nitrogen dioxide exposure with bronchial reactivity have been conducted. The first, including studies up to the early 1990s, showed that there was a statistically significant increase in airway hyperresponsiveness to a range of constrictor stimuli following nitrogen dioxide exposure (> 200 μg/m^3 in asthmatics and > 1900 μg/m^3 in healthy controls) *(129)*. A more recent systematic review considered peer-reviewed and non-peer-reviewed original research published up to 2009 and included 41 exposure scenarios from 28 studies *(130)*. Provoking agents included methacholine, histamine, carbachol, cold air and allergens. Nitrogen dioxide exposure was considered in categories of 188–375 μg/m^3, 376–563 μg/m^3, 564–751 μg/m^3, 752–939 μg/m^3, 940–1127 μg/m^3 and 1128–1316 μg/m^3. Overall exposure was associated with increases in airway reactivity and in stratified analyses, associations of bronchial reactivity with exposure were seen within each of the two lowest exposure categories. There was no clear dose–response relationship between the categories. The authors felt the lack of a dose–response effect suggested that nitrogen dioxide did not cause these effects, and that the effect size was too small to be of clinical significance. The lack of a clear dose–response effect is difficult to explain and would argue against a causal relationship. However, for some of the analyses conducted the results are remarkably consistent across studies (I^2 = 0% for the fraction of asthmatics with greater airway hyperresponsiveness following nitrogen dioxide exposure in the lowest and second lowest exposure categories). The small significant increase in airway reactivity associated with low-level exposure could, if borne by a large

proportion of the population, be associated with population-level health effects.

- Included in the meta-analysis by Goodman et al. *(130)* are studies suggesting that exposure to nitrogen dioxide may reduce the threshold of responsiveness to inhaled allergen in those who are sensitized. There was no evidence that the effect of nitrogen dioxide on these specific airway challenges was any different from its effect on response to nonspecific agents. One of the earliest studies to look at this showed that asthmatics sensitized to house dust mites, exposed for 60 minutes to 752 μg/m^3 nitrogen dioxide, had significantly larger falls in FEV_1 in response to house dust mite challenge compared to exposure to air *(131)*. A similar effect was observed in pollen-sensitized asthmatics exposed for 30 minutes to 490 μg/m^3 nitrogen dioxide and then exposed to pollen. After exposure, the falls in peak flow were larger (6.6% difference) and more asthmatics experienced a late asthmatic response, although this latter difference was non-significant *(132)*. Repeated daily exposures of 500 μg/m^3 for 30 minutes for 4 days increased the early- and late-phase falls in FEV_1 following low-dose allergen exposure *(133)*. Simultaneous exposure to nitrogen dioxide (752 μg/m^3) and sulfur dioxide for 6 hours has also been demonstrated to increase response to allergen *(134,135)* . Repeated 30-minute exposures to 500 μg/m^3 nitrogen dioxide are associated with a more pronounced eosinophilic response to allergen challenge, as demonstrated by elevated levels of eosinophilic cationic protein in bronchial washings *(136)* and in sputum and blood *(137)*.
- Exposure to 1880 μg/m^3 nitrogen dioxide for three hours followed by analysis of bronchial lavage fluid has shown that markers of airway inflammation were altered (decreased 6-keto-prostaglandin, increased thromboxane B2 and prostaglandin D2) in those with mild asthma. This was not seen in healthy volunteers, and not seen after exposure to filtered air *(138)*.

Another approach is to directly examine health effects following exposure to cooking with gas. In a chamber study, nine adults and eleven children with asthma were exposed to nitrogen dioxide alone and then nitrogen dioxide with combustion products from a gas heater for a one-hour period *(139)*. Symptoms, lung function and airway reactivity were monitored. Small, clinically non-significant increases in airway reactivity were seen on exposure to 1128 μg/m^3, but this was not seen when exposure occurred with combustion products. The authors concluded these exposures were not associated with clinically relevant health effects.

Overall, these controlled human clinical studies, many of which were conducted more than 20 years ago, have examined the health effects of acute and often very high levels of exposure to nitrogen dioxide rather than the chronic, low-dose exposures experienced by most human populations. Notwithstanding

this, however, they suggest that those who are sensitized or who have asthma may be at particular risk of health effects from exposure to nitrogen dioxide at levels that may be experienced for short periods when individuals are near an unvented combustion appliance.

Epidemiological studies

Identification of studies

Epidemiological studies on health effects of indoor nitrogen dioxide exposure were identified from several electronic searches and by hand searching references in former reviews by WHO *(15)* and EPA *(107)*. Electronic searches were made in PUBMED (http://www.ncbi.nlm.nih.gov/pubmed/), in the ISI Web of Science (http://apps.isiknowledge.com/) and in the LUDOK literature database on air pollution and health effects (http://www.ispm-unibasel.ch/ludok/welcome.html) in January 2009.

We intended to identify all studies with original data on health effects with indoor nitrogen dioxide measurements, and the main descriptors used were "air pollution, indoor", "nitrogen oxides", and "morbidity" or "mortality". We excluded studies that referred to solid fuel use, as this source is often also associated with high levels of particulate matter. We also excluded studies with purely descriptive results or in which no attempt had been made to adjust for potential confounders. In December 2009, a similar search strategy was adopted in order to identify reports published during the period of the review.

We found 72 studies with indoor measurements and evaluation of health effects up to January 2009. Three of these were related to the same study, and here we used the newer results or the publication with the analysis of the most complete sample.

An update of the search found two more publications up to December 2009. Among the remaining 71 studies, we focused on 35 studies on respiratory symptoms and disease, because this outcome was most often significantly related to nitrogen dioxide exposure and permitted the evaluation of concentrations for setting guidelines. Of these 35 studies, 20 were in children, 5 in adults and 10 in asthmatics (children and adults).

In addition, studies that examined the health effects of indoor gas appliances were identified through hand searches of earlier reviews of the topic, citations within the papers identified on health effects of nitrogen dioxide, and papers known to the expert group. We also searched for epidemiological studies on health effects of indoor gas combustion without measurements with the terms "air pollution, indoor", "gas" with "cooking" or "heating", and "respiratory tract diseases" or "lung function".

As there has been some concern that susceptibility may vary with age, the epidemiological studies are presented in two sections – studies in children and studies in adults.

Epidemiological studies in children

Estimates of health effects from studies in which direct measurements of indoor nitrogen dioxide have been made are included in Table 5.2 (see page 280).

Health effects in infants: studies measuring indoor nitrogen dioxide. There have been concerns that infants may be at particular risk of symptoms with high indoor nitrogen dioxide levels because of their high minute volume in relation to body size and because they are likely to spend a large proportion of their time indoors.

However, an early longitudinal study of over 1000 infants up to the age of 18 months living in non-smoking homes showed that the incidence of respiratory illness was not associated with two-week average bedroom nitrogen dioxide levels (22% of nitrogen dioxide levels measured were > 37.6 μg/m^3) *(140)*.

A large cross-sectional study of infants aged 3–12 months taking part in a birth cohort study showed no association of two-week average bedroom nitrogen dioxide (median 12.7 μg/m^3) with respiratory symptoms, including cough, breathlessness and wheezing. Of the 20 infant symptoms examined, only diarrhoea was associated with indoor nitrogen dioxide levels (adjusted odds per doubling of 1.38; 95% CI 1.11–1.70) *(141)*.

More recently, a nested case control study of infants taking part in a birth cohort study was conducted in Oslo, where gas appliances are not used indoors for heating or cooking and levels of indoor nitrogen dioxide are low *(142)*. No association of bronchial obstruction (wheezing, chest recession, rhonchi during auscultation of the chest, forced expiration or rapid breathing, with at least one other episode of "obstructive airways disease") in the first two years of life at living room levels of nitrogen dioxide (arithmetic mean 14.7 μg/m^3; range 2–43 μg/m^3) was seen in 153 matched pairs of cases and controls. However, data from a birth cohort study in Sweden (where, again, indoor gas appliances are rare), using a similar nested case control design, suggested an association of recurrent wheezing up to the age of two years with mean four-week living room nitrogen dioxide *(143)*. There was an increased risk (OR 1.48; 95% CI 0.91–2.42) of wheeze comparing the highest quartile (> 15.6 μg/m^3) to the lowest quartile (< 8.4 μg/m^3), with little evidence of an association below 15.6 μg/m^3. However, the reported associations are below conventional levels of statistical significance. Another study in Scandinavia, but this time based in Copenhagen, showed no association of bedroom nitrogen dioxide levels (mean level 8.6 μg/m^3; 5th centile 3.3 μg/m^3; 95th centile 17.0 μg/m^3, based on up to three ten-week periods of monitoring) with symptoms of wheeze in almost 400 infants born to asthmatic mothers in the first 18 months of life *(144)*.

Populations of infants with higher exposure to indoor nitrogen dioxide were examined in a three-centre birth cohort study. Two-week average (median and 75th centile) living room nitrogen dioxide in each of the three centres (Ashford,

Kent, United Kingdom 10.7 and 16.5 μg/m^3; Barcelona, Spain 86.2 and 112.0 μg/m^3; Menorca, Spain 22.2 and 39.9 μg/m^3) was not associated with wheeze, cough, chestiness or doctor-diagnosed respiratory illness in the first year of life *(145)*. Researchers in the Menorca centre went on to examine associations of neurocognitive status in four-year-old children with level of exposure to nitrogen dioxide as measured at three months *(146)*. A negative association of poor cognition with nitrogen dioxide was observed (a decrease of 0.27 points on a standardized McCarthy Scale measure of cognition per 1.88 μg/m^3). Further, children with increased exposure were at a higher risk of having symptoms of inattention (6% increased risk per 1.88 μg/m^3 increase in nitrogen dioxide). This was particularly seen in children with the GSTP1–Val 105 allele, a genetic polymorphism that may lead to reduced antioxidant defences within the developing brain. In this study, over 70% of children lived in homes with a gas cooker, and almost a quarter had gas fires. The authors stated that confounding by other pollutants such as particulates could not be ruled out, particularly as many of the homes were using bottled gas. Unfortunately, the other centres taking part in the study do not have the necessary outcome information to try to replicate this observation.

Two publications based on a longitudinal study of infants in Connecticut examined lung health and its association with indoor gas appliances and indoor nitrogen dioxide levels *(40,147)*. Participants were selected if, at birth, their mother reported she had another child under the age of 11 years who had asthma. In the 850 infants included in the first report, living in a home with a gas stove was associated with an increased risk of persistent cough (OR 1.52; 95% CI 1.06–2.18) after adjustment for maternal education and a range of household factors including allergen levels, mould and mildew, and smoking in the home. These children had asthmatic siblings and might be considered to be a genetically susceptible group, but the associations were only seen in children whose mother did not have asthma. Forty-five per cent of the infants were living in homes with a two-week average living room nitrogen dioxide level greater than 18.8 μg/m^3, and an association of nitrogen dioxide level with persistent cough was also reported (1.21; 95% CI 1.05–1.40 per 18.8-μg/m^3 increase). In the second report, mothers of about 750 newborn infants recorded each day their infants' respiratory symptoms during the first year of life. Two-week mean living area nitrogen dioxide was measured concurrently with nitrous acid (interquartile range 9.6–32.7 μg/m^3 for nitrogen dioxide, 1.1–4.2 ppb for nitrous acid). In single-pollutant models, a dose-dependent association of the number of days with wheeze, cough and shortness of breath was observed in these infants. Observed associations were most marked for shortness of breath. The adjusted rate ratio for shortness of breath in those with nitrogen dioxide levels > 32.7 μg/m^3 compared to those with levels below 9.6 μg/m^3 was 2.38 (95% CI 1.31–4.38) after adjustment for nitrous acid level. No independent association of symptoms with nitrous acid was seen.

Health effects in children: studies measuring indoor nitrogen dioxide. One of the earliest studies to measure indoor nitrogen dioxide was conducted in the United Kingdom *(148)*. Children living in homes that cooked with gas had more ($P > 0.06$) respiratory illness (positive response to any of cough, wheeze, colds that went to the chest, or asthma or bronchitis in the previous 12 months). In the children who lived in gas-cooking homes, the prevalence of respiratory illness increased with increasing bedroom nitrogen dioxide level: 44%, 59% and 71%, respectively in those exposed to 0–37.6 μg/m^3 , 37.6–75.2 μg/m^3 and 75.2 μg/m^3 ($P < 0.05$). No association of $FEV_{0.75}$, peak flow or mean mid-expiratory flow rate with indoor level of nitrogen dioxide was observed.

Cross-sectional studies were conducted in the Netherlands, where there was concern over the combustion products produced by gas water heaters or geysers. In a study of over 1000 children, no association was observed between respiratory symptoms and lung function measurements (FEV_1, FVC, PEFR, MMEF) and household weekly average nitrogen dioxide level (mean levels 23.6 μg/m^3 for homes without geysers, 40.3 μg/m^3 for homes with vented geysers and 71.7 μg/m^3 for homes with unvented geysers) *(149,150)*.This supported earlier work in the Netherlands showing no association of indoor nitrogen dioxide level with respiratory symptoms *(151)*.

Garrett et al. *(152)* studied children living in Victoria, Australia over a one-year period. Indoor nitrogen dioxide was measured on five occasions in three locations in the home and the frequency recorded of eight respiratory symptoms during the year of observation. Respiratory symptoms were associated with the presence of a gas stove but not with any of the other sources of indoor nitrogen dioxide (gas heaters or smoking in the home). Respiratory symptoms, but not peak flow variability, were more frequent in children with higher bedroom levels of nitrogen dioxide but not kitchen or lounge levels (adjusted odds for any of eight possible respiratory symptoms with bedroom average level > 20 μg/m^3 = 3.62 (95% CI 1.08–12.08) compared to < 10 μg/m^3). The association of respiratory symptoms with a gas stove persisted even after adjustment for bedroom nitrogen dioxide, raising the possibility that the association with gas appliances was not explained by exposure to this pollutant. Interestingly, both the presence of a gas stove and bedroom nitrogen dioxide level were non-significantly more strongly associated with respiratory symptoms in atopic children than in non-atopic children.

In some parts of the world, children's exposure to gas combustion products may be determined or at least strongly influenced by their exposure to gas heaters at school. This has been investigated in Australia. School levels of nitrogen dioxide were monitored during the winter, as were the personal levels of nitrogen dioxide in children who lived in homes with gas sources *(27)*. The winter average six-hourly mean nitrogen dioxide levels in classrooms with an unflued gas heating source ranged from 33.8 to 248 μg/m^3 compared to 13.2–43.2 μg/m^3

in rooms without a gas heater. Several symptoms were investigated (hoarseness, cough with phlegm, dry cough, sneeze, stopped up nose, runny nose, wheeze, sore throat, colds and school absence) but only the mean symptom rate for the latter three showed consistent and significant associations with exposure to > 150.4 μg/m^3 compared to 37.6 μg/m^3. There was some evidence of a dose–response relationship.

One of the most comprehensive assessments was conducted as part of the Six City study. The association of respiratory symptoms with indoor nitrogen dioxide level was examined in more than 1500 children *(153)*, who were followed up for one year. About half of the children lived in homes with a major source (gas stove or kerosene heater). Household annual average levels were determined based on summer and winter measurements made in three household locations, and were 16.1 μg/m^3 for homes without a source and 44.2 μg/m^3 for homes with a source. At the end of follow-up, the annual cumulative incidence of any lower respiratory symptom (shortness of breath, chronic wheeze, chronic cough, chronic phlegm or bronchitis) was higher in those children living in homes with a source (29.0% vs 22.8%) and was higher with increasing annual average indoor nitrogen dioxide (1.40; 95% CI 1.14–1.72 per 28-μg/m^3 increase). Household particulate matter ($PM_{2.5}$) was also measured in this study and included as a covariate in the final analysis. The observed association of incidence of symptoms with both the presence of a gas stove and with increasing indoor nitrogen dioxide level persisted after adjustment for the indoor particle level. In this study, no consistent association of lung function with source or measured nitrogen dioxide was observed. Further analyses were conducted later using regression calibration to include information from children who were not directly measured for nitrogen dioxide but who did have information on surrogate factors such as the presence of a gas appliance *(154)*. Although the authors argued that the estimate, now based on more than 2800 children, was 34% more precise, the effect estimate was little different to earlier analyses (risk of lower respiratory illness over one year, OR 1.5; 95% CI 1.2–1.8 per 28 μg/m^3 increase).

A detailed longitudinal study of the health effects of indoor and outdoor nitrogen dioxide was conducted in schoolchildren in Japan, a country in which the use of gas for cooking is almost universal and where some homes use unvented gas appliances for heating *(10)*. Indoor measurements of nitrogen dioxide were made in summer and winter (mean of the two measurements in homes with vented and unvented appliances were 34.5 and 60.9 μg/m^3, respectively) and outdoor nitrogen dioxide measurements were made at a sampling station based at the child's school (three-year average in each of the six areas involved ranged from 13.2 to 58.3 μg/m^3). There was no association of respiratory symptoms with exposure to gas heaters. At baseline in girls (but not boys), significant associations of indoor nitrogen dioxide with wheeze (OR 1.90; 95% CI 1.30–2.83 per 18.8 μg/m^3), asthma (OR 1.63; 95% CI 1.06–2.54 per 18.8 μg/m^3) and a history of

bronchitis (OR 1.42; 95% CI 1.06–1.90 per 18.8 μg/m^3) were observed even after adjustment for outdoor levels. However, over a three-year period there was no evidence that indoor nitrogen dioxide was associated with incidence of disease, although associations were seen with outdoor nitrogen dioxide level.

Health effects in children: studies measuring personal nitrogen dioxide. Some studies have measured personal nitrogen dioxide rather than indoor levels. The extent with which personal nitrogen dioxide reflects exposure to indoor, compared to outdoor, nitrogen dioxide will vary depending on the time-activity patterns of the child and the frequency and duration of use of indoor sources.

Personal exposure to nitrogen dioxide was measured in children in Hong Kong SAR *(155)*, where indoor sources are common. No association of exposure with symptoms was observed. However, personal exposure was strongly influenced by outdoor levels, with significant differences in personal exposure seen in children who wore samplers during a week of high ambient nitrogen dioxide (40.2 μg/m^3) and those who wore them during a week with lower levels (33.4 μg/m^3).

Personal nitrogen dioxide exposure was measured in 3–4-year-old children in Quebec City, Canada during the winter months and a dose-dependent association of exposure with asthma was reported. Only 6 of the 140 children lived in a home with a gas stove (mean personal exposure with gas stove 32.4 μg/m^3; without gas stove 17.3 μg/m^3). The adjusted OR for case status with the highest level of exposure appears unrealistically high, with very wide confidence levels (24-hour mean of 28.2 μg/m^3 compared to "a zero level"). The unmatched analysis OR was 19.9 (95% CI 4.75 –83.03) while the matched analysis OR was 10.55 (95% CI 3.48 –31.89) *(156)*; this was probably related to the small numbers of children in the risk group.

Personal nitrogen dioxide samplers were worn by Australian primary school children living in Canberra, a low pollution area *(157)*. They were worn from the end of the school day till the following morning, and if the child was taught in a classroom with a gas heater, classroom levels were also measured. Average total personal exposure was low (19.0 μg/m^3) and was not associated with changes in lung function, except for a slightly more pronounced response to a cold air challenge (as measured by change in FEV_1/FVC). There was some evidence that this association was more apparent in children who were *not* mite-sensitized.

One-week average personal exposure was measured in 163 preschool children in Finland *(158)* who attended one of eight day care centres. A small proportion (9.2%) lived in homes with gas appliances (study median 21.1 μg/m^3). However, there was an increased risk of reported cough during the same week as measurement (≤ 16.2 μg/m^3 reference group; 16.2–27.2 μg/m^3, RR 1.23, 95% CI 0.89–1.70; and ≥ 27.2 μg/m^3, RR 1.52, 95% CI 1.00–2.31), particularly in the winter. No clear association with peak expiratory measurements in a subsample

of children (n = 53) was seen. Data from the same study were re-analysed using several methods of defining nitrogen dioxide exposure *(159)*. Overall, statistically significant associations of cough were seen only with personal exposure and in winter, although the direction of association with levels of nitrogen dioxide measured inside the day care centre, outside the day care centre and at a local fixed site was consistent with this observation.

Health effects in children with asthma: studies measuring indoor or personal nitrogen dioxide. Several studies have examined nitrogen dioxide exposure in relation to symptoms of asthma in those with established disease. All have observed increases in some symptoms, but some of the observed associations have not been consistent across the whole population under study.

In Adelaide, Australia, 125 asthmatics wore lapel nitrogen dioxide monitors each day for six weeks while they were at home and kept a symptom diary *(160)*. Time-averaged level of personal exposure to nitrogen dioxide in the home was strongly related to the presence of gas appliances, particularly those in homes with unflued heating appliances (mean average exposure 125 $\mu g/m^3$; interquartile range 50.7–310 $\mu g/m^3$) compared to those in homes using all electric appliances (22.6 $\mu g/m^3$; interquartile range 20.7–28.2 $\mu g/m^3$). In participants under the age of 14 years, there was an association of personal exposure level with symptoms of chest tightness (OR 1.29; 95% CI 1.16–1.43 per standard deviation increase in nitrogen dioxide, which in this study was 48.3 $\mu g/m^3$), breathlessness (OR 1.13; 95% CI 1.0–1.28 with a one-day lag) and asthma attacks. In adults, only one isolated association of one of the seven symptoms investigated was associated with nitrogen dioxide, and this was seen only after accounting for a one-day lag.

Personal exposure to nitrogen dioxide was measured in 45 asthmatic children over a 10-day period by Delfino et al. *(161)* in Seattle. The children, aged 9–18 years, were also subject to daily measurements of airway inflammation (exhaled nitric oxide) with a personal active sampling device. Increases in fractional exhaled nitric oxide (FENO) were seen with $PM_{2.5}$, elemental carbon and nitrogen dioxide (for each 32-$\mu g/m^3$ increase in nitrogen dioxide, an increase of 1.6 ppb FENO (95% CI 0.4–2.8)). Positive associations were seen only in those who were taking anti-inflammatory medication, which may reflect the severity of the underlying disease. In this population, there was a wide range of personal exposure (5.1–198.7 $\mu g/m^3$). Daily lung function measurements were also made *(162)*. Personal nitrogen dioxide was associated with decrements in lung function, the change in FEV_1 as a percentage of predicted FEV_1 being 2.45 (95% CI 3.57 –1.33) per 32-$\mu g/m^3$ increase in nitrogen dioxide. Lung function associations were more clearly seen in those children who did not use a bronchodilator. These associations were robust to adjustment for personal $PM_{2.5}$ exposure, but the authors in their discussion suggest that the association with nitrogen dioxide may be due to confounding by another toxic pollutants from traffic.

A larger study conducted in eight inner-city areas in the United States (Bronx, NY; East Harlem, NY; St Louis, MO; Washington, DC; Baltimore, MD; Chicago, IL; Cleveland, OH; and Detroit, MI) recruited children attending accident and emergency departments for the treatment of asthma, measured indoor nitrogen dioxide in the children's bedrooms (median 56.0 μg/m^3; range 0.9–902.4 μg/m^3) and gathered health information at baseline and three, six and nine months later *(23)*. Three respiratory outcomes were considered: (*a*) more than four days in the last fortnight with symptoms; (*b*) unscheduled visits to health care providers; and (*c*) peak flow less than 80% of predicted. Associations of these outcomes with nitrogen dioxide were modified by atopic status and by season. Nitrogen dioxide levels in the highest quartile (cut-off not given) were associated with more than four days with symptoms compared to those exposed to lower levels, but this was only in children who had *negative* skin tests. No association was seen in those who were skin-test-positive to at least one of 16 common indoor and outdoor aero-allergens. The overall difference in indoor nitrogen dioxide level in warm and cold months was relatively small (6.8 μg/m^3) but low peak flow was associated with nitrogen dioxide only in the colder months. The authors postulate that this may reflect increased susceptibility to infections during the colder months. However, as children spend more time indoors when it is cold, the association may have arisen because of the closer correlation of indoor measurements with personal measurements in the winter period.

A total of 150 inner-city children with asthma, predominantly African Americans, were studied over a six-month period in Baltimore, United States *(26)*. Although at baseline the average indoor nitrogen dioxide level was similar in the homes of asthmatic children and a control group of non-asthmatic children *(163)*, there was evidence that indoor nitrogen dioxide was associated with symptoms in the asthmatic children. Assessment of bedroom indoor nitrogen dioxide and indoor $PM_{2.5}$ was made on three occasions (overall mean of average seven-day indoor nitrogen dioxide 56.4 μg/m^3) and caregivers were asked to report symptoms that had occurred in the previous fortnight. There was a significantly increased risk of reporting symptoms with increasing nitrogen dioxide levels (e.g. adjusted incident rate ratio for speech-limiting wheeze 1.17 (95% CI 1.08–1.27) per 37.6-μg/m^3 increase in nitrogen dioxide) and these associations were present even after adjustment for indoor particulates. No association was observed for other outcomes such as medication use or use of health services. About two thirds of the children were atopic as assessed by skin tests, but in general the presence of atopy did not modify the associations observed. However, nocturnal symptoms were more strongly related to nitrogen dioxide levels in atopic children (incidence rate ratio 1.13 per 37.6 μg/m^3 increase in nitrogen dioxide) compared to non-atopic children (incidence rate ratio 1.03 per 37.6 μg/m^3 increase in nitrogen dioxide). About 83% of these homes had gas stoves for cooking and 12% reported they used their stove for heating the home.

The association of symptoms in children with asthma with the use of gas appliances and indoor nitrogen dioxide level may be different in different housing conditions. In Connecticut and south-west Massachusetts in the United States, the reporting of wheeze and chest tightness in the month prior to indoor nitrogen dioxide sampling (mean 10-day average living room nitrogen dioxide 16.2 $\mu g/m^3$ in homes without a source and 48.7 $\mu g/m^3$ in homes with a source) in children with asthma was significantly associated with the presence of a gas stove and with increases in nitrogen dioxide levels as measured in the main living area. However, this association was only seen when analyses were limited to children living in homes that were in "multi-family" housing and were not seen in single-family housing *(164)*. Among these children in multi-family homes, exposure to gas stoves increased the likelihood of wheeze (OR 2.27; 95% CI 1.15–4.47), shortness of breath (OR 2.33; 95% CI 1.12–5.06) and chest tightness (OR 4.34; 95% CI 1.76–10.69) and each 37.6-$\mu g/m^3$ increase in nitrogen dioxide increased both likelihood of any wheeze (OR 1.52; 95% CI 1.04– 2.21) or chest tightness (OR 1.61; 95% CI 1.04– 2.49), and days of wheeze (RR 1.33; 95% CI 1.05–1.68) or chest tightness (RR 1.51; 95% CI 1.18–1.91). These multi-family homes were smaller, the implication being that main living room levels of nitrogen dioxide may better reflect the child's bedroom level. Multi-family homes had higher levels of nitrogen dioxide (45% recording two-week averages of > 37.6 $\mu g/m^3$ compared to only 9.3% in the single-family homes). Children included in this study were the siblings of the infants recruited into the study reported by Belanger et al. *(147)* and Van Strien et al. *(40)* and described earlier in this chapter.

One possible mechanism to explain the association of indoor nitrogen with asthma may be an increased susceptibility to severe or prolonged infection. In England, 112 children with asthma were followed up for almost a year, during which period they kept an asthma diary and measured their personal exposure over each seven-day period using Palmes tubes *(165,166)*. When asthma exacerbations occurred, nasal aspirates were taken to confirm the presence of a viral infection.

The geometric mean exposure to nitrogen dioxide at the time of infection was 10.6 $\mu g/m^3$. Compared with exposures of < 8 $\mu g/m^3$, exposures of > 28 $\mu g/m^3$ were associated with an increased risk of asthma following infection (RR 1.9; 95% CI 1.1–3.4). The risk of experiencing an episode of lowered peak expiratory flow after having experienced symptoms highly suggestive of infection increased in a dose-dependent fashion with increasing nitrogen dioxide levels at the time of the infection. The increase in symptom score and the decrements in peak flow experienced during the laboratory-confirmed viral infection were larger in children who had higher exposures measured in the week prior to the start of the exacerbation. Although the average personal nitrogen dioxide was lower than in some studies, it was strongly related to the presence of gas appliances in the home and 23 of the children had at least one measurement in

excess of 100 μg/m^3 (32 of the measurements of the seven-day average personal exposure were > 100 μg/m^3).

These observations that children with asthma have worse symptoms if exposed to higher levels of indoor nitrogen dioxide suggest that their removal from exposure should lead to amelioration of their symptoms. However, few interventional studies have been reported. In recognition that classroom levels of nitrogen dioxide (largely determined by the use of unflued gas heaters) are an important source of exposure, an intervention study was conducted in Australia. Researchers assessed the effect of changing from unflued gas heaters in school classrooms to flued gas heaters or electric heaters *(167)*. Almost 200 asthmatic children in 10 control schools, 4 schools that had changed to flued gas heaters and 4 schools that had changed to electric heaters were followed for a period of 12 weeks. Following the intervention, the mean rate of symptoms of difficulty breathing during the day and at night, chest tightness and asthma attacks during the day was lower in children attending intervention schools. No change in lung function parameters was observed. Six-hourly average classroom levels of nitrogen dioxide ranged from 13.2–71.4 μg/m^3 (intervention) to 22.5–218.1 μg/m^3 (control) during the period of follow-up.

In further studies, 174 of these children with asthma kept a symptom diary over a 12-week period *(168)*. Home (kitchen) and classroom nitrogen dioxide levels were measured (indoor daily range: classroom 16.9–577.2 μg/m^3; kitchens 5.6–795.4 μg/m^3) and the association of several symptoms with the maximum of three daily time-averaged kitchen and classroom levels was assessed. Difficulty in breathing at night was associated with school (adjusted relative rate 1.11 (95% CI 1.05–1.18) per 18.8- μg/m^3 increase in nitrogen dioxide) and home levels (adjusted relative rate 1.03 (95% CI 1.01–1.05) per 18.8 μg/m^3 increase), while associations with nocturnal chest tightness and nocturnal asthma were seen only for school (adjusted relative rate 1.12 (95% CI 1.07–1.17) per 18.8-μg/m^3 increase in nitrogen dioxide) and home level (adjusted relative rate 1.04 (95% CI 1.00–1.07) per 18.8-μg/m^3 increase), respectively. Decrements in lung function (mean FEV_1 % predicted) were observed (–0.39% per 18.8 μg/m^3 increase in nitrogen dioxide level in the kitchen). At the time of the study, mattress house dust mite levels were assessed; there was no evidence that the association of nitrogen dioxide with symptoms was modified by mattress allergen levels.

Another intervention study was conducted in New Zealand *(169)*. Parents of children with asthma, living in homes heated by an unflued gas heater or a plug-in electrical heater, were invited to alter their current heating system to either a heat pump, a wood pellet burner or a flued gas heater. All eventually received their heater of choice, but they were randomized to receive them immediately (treatment group) or after one year (control group).

Improvements in subjective markers of health as reported by parents (sleep disturbed by wheeze, dry cough at night, overall health) symptoms reporting

in diaries (cough at night, wheeze at night) and health service utilization (visits to the doctor, visits to the pharmacist) were seen in the treatment group but no change in objective markers such as peak flow variability or lung function tests were seen. During the period of the study, the levels of nitrogen dioxide in the bedrooms and living rooms of the intervention group were 8.5 and 7.3 μg/m^3, respectively, compared with the levels in the control group of 15.7 and 10.9 μg/m^3, respectively (both $P > 0.001$). However, the intervention houses were also warmer (0.57 °C and 1.1 °C for the bedroom and living room, respectively) and therefore health status may have been higher owing to increased warmth rather than decreased nitrogen dioxide levels.

The Hasselblad meta-analysis. In the early 1990s, Hasselblad et al. published a meta-analysis of the association of indoor nitrogen dioxide levels with respiratory illness in children *(170)*. This report was one of the earliest examples of the use of meta-analysis for synthesizing evidence from studies of environmental hazards. It included published studies that had measured either indoor nitrogen dioxide or the use of a gas appliance as the exposure metric and combined the results from 11 studies, presented in 15 different publications from the Netherlands *(150,171)*, the United Kingdom *(148,172–178)* and the United States *(153,179–182)*.

In studies in which gas stoves rather than measured nitrogen dioxide represented the exposure, it was assumed that the average nitrogen dioxide exposure was about 30 μg/m^3 higher in homes with a gas stove than in those without one. Respiratory symptoms were any respiratory symptom, with some variation between studies but including wheeze, cough, coughs going to the chest, shortness of breath and bronchitis. In children under the age of 12 years, a 30-μg/m^3 increase was equivalent to a 20% increased risk of symptoms. Exclusion of studies in which gas stoves were the proxy markers for exposure led to an increase in effect size (OR 1.27 per 30-μg/m^3 increase). This analysis is of considerable importance, as it provided the basis for outdoor air quality guideline setting by WHO in 1997 *(183)* and its conclusions have, to date, not been seriously challenged by any new evidence. Extrapolating directly from the Hasselblad meta-analysis, WHO in 1997 reported that "On the basis of a background level of 15 μg/m^3 (0.008 ppm) and the fact that significant adverse health effects occur with an additional level of 28.2 μg/m^3 (0.015 ppm) or more, an annual guideline value [for outdoor nitrogen dioxide] of 40 μg/m^3 (0.023 ppm) is proposed. This value will avoid the most severe exposures."

Epidemiological studies in adults

In comparison to the number of studies in children, there are relatively few studies that have reported associations of adult respiratory health with indoor nitrogen dioxide levels.

Health effects in adults: studies measuring indoor nitrogen dioxide. Indoor nitrogen dioxide measurements were made in a subsample of households taking part in a longitudinal study in the United States (mean 24-hour average 94.0 μg/m^3 in homes using gas for cooking and 37.6 μg/m^3 in those using electricity). No association of respiratory illness in any member of the household (including adult members) with measured nitrogen dioxide level was observed *(180)*.

A cohort of 152 non-smoking women living in Vlagtwedde and Vlaardingen in the Netherlands was studied in 1982. Time-activity patterns showed that the women spent about 25% of their time in their kitchens, 25% in the lounge and 35% in the bedroom *(184)*. Most (97) of the women had also had their FEV_1 measured and, in general, decrements in FEV_1 were associated with increases in indoor nitrogen dioxide levels, the largest estimates being seen for measurements in the bedroom (mean deficit in FEV_1 2.38 ml per μg/m^3 increase in nitrogen dioxide; $P < 0.01$) and the lounge (mean deficit in FEV_1 3.91 ml per μg/m^3 increase in nitrogen dioxide; $P > 0.05$) rather than the kitchen (mean deficit in FEV1 0.69 ml per μg/m^3 increase in nitrogen dioxide; $P > 0.05$) *(185)*. Although there was some evidence that increasing nitrogen dioxide level was associated with the decline in FEV_1 that had been recorded in these women over the previous 13 years, this association failed to reach conventional levels of significance. Effect modification by atopy or asthma was not considered.

In Hong Kong SAR, mothers of children taking part in a large study of respiratory health wore personal nitrogen dioxide badges for a 24-hour period *(155)*. Personal nitrogen dioxide was higher in women if they cooked more frequently, but only among those who did not ventilate their kitchen by the use of an extractor fan. In users of LPG or kerosene, the mean personal 24-hour average exposure was 37.7 μg/m^3 if the kitchen was ventilated during cooking and 41.7 μg/m^3 if the kitchen was unventilated. There was no consistent association of personal nitrogen dioxide with frequency of cooking or presence of ventilation fans in the children living in these homes, probably reflecting their different time-activity patterns. Personal nitrogen dioxide was higher in women who cooked with LPG compared to those using piped gas.

There was some evidence that personal exposure levels may be associated with chronic cough and allergic rhinitis. The mean personal 24-hour average exposure was 42.3 μg/m^3 in women with cough and 35.9 μg/m^3 in those without ($P = 0.05$), while it was 42.4 μg/m^3 in women with allergic rhinitis and 35.5 μg/m^3 in those without ($P = 0.002$).

Women who had recently given birth were recruited into a study in which health information was collected at baseline and the presence of respiratory symptoms regularly collected every two weeks for a year *(186)*. Indoor nitrogen dioxide measurements were made with passive samplers over a two-week period in the winter and this was repeated depending on whether gas or kerosene appliances were present. Even though this was a large study involving 888

non-smoking women, no association of nitrogen dioxide level with symptoms of wheeze, chest tightness, hoarseness or phlegm was seen when nitrogen dioxide was considered as a continuous variable. When it was dichotomized, however, to compare the top quartile (> 150.4 μg/m^3) with the lower three quartiles, household levels were associated with chest tightness (1.94; 95% CI 0.98–3.85) and with wheeze (4.00; 95% CI 1.45–11.0). An association of symptoms with the use of kerosene heaters was reported and this may have been due to the sulfate emissions from these heaters.

Indoor nitrogen dioxide levels were measured for one week in the homes of 148 people with severe COPD living in north-eastern Scotland *(187)*. Half of the homes had at least one active smoker, and nitrogen dioxide levels were higher in homes with smokers (median 16.2 μg compared to 12.9 μg; $P < 0.02$) and no association of symptoms or specific respiratory quality of life was observed.

Kitchen, living room and bedroom nitrogen dioxide levels were measured for one week in the summer and one week in the winter in urban (Pisa) and rural (Po Delta) areas of Italy *(188)*. Mean kitchen levels of nitrogen dioxide were statistically different in the two regions (54.5 vs 62.0 μg/m^3 ($P < 0.05$) in winter and 41.4 vs 37.6 μg/m^3 ($P < 0.01$) in the summer for Pisa and the Po Delta, respectively). An average personal exposure in adults was generated from time-activity patterns. Exposure above the study median nitrogen dioxide index was associated with an increased risk of acute respiratory symptoms (OR 1.66; 95% CI 1.08–2.57) but no association was seen for bronchitic/asthmatic symptoms.

Those who cook in the home and professional cooks are exposed to high levels of nitrogen dioxide as well as to other cooking-related pollutants. There is no evidence from large-scale epidemiological studies that have measured indoor nitrogen dioxide levels that respiratory health is worse in those who regularly use unvented gas appliances for cooking. In a cross-sectional study of 37 professional cooks (mainly women) working in four large hospital kitchens in Brazil *(189)*, average daily levels of nitrogen dioxide in one kitchen reached almost 188 μg/m^3. The authors presented tabulated coefficients from regression models to suggest total exposure to nitrogen dioxide (the product of years working in that kitchen times the level of nitrogen dioxide in the kitchen) was associated with lower levels of forced expiratory flow ($P < 0.031$), even after adjustment for smoking behaviour and the presence of asthma, but it is difficult to interpret the effect estimates from this. Confounding by other cooking-related pollutants cannot be ruled out.

Presence of gas appliances at home as an indicator of nitrogen dioxide exposure

In setting guidelines for indoor air quality, there is clearly a need for direct measurements of nitrogen dioxide levels, and for these levels to be associated with some health impairment. In the indoor setting, however, where the source of indoor nitrogen dioxide may, in the main, be from indoor gas appliances, the pres-

ence of the appliance itself may act as a proxy marker of exposure. Of particular concern is that the use of some appliances, particularly gas cookers (which are unvented) is associated with short-lived peaks of exposure that are not captured or measured by most of the monitoring techniques used in epidemiological studies. Controlled exposure studies suggest that nitrogen dioxide at levels associated with these peaks may be harmful but studies that use "average nitrogen dioxide" may not be able to detect these health effects. Under these circumstances, association of a health effect with the presence and use of the gas appliance may provide stronger evidence of health effects of indoor nitrogen dioxide than measurements of the gas itself.

However, there are three major pitfalls with this approach. First, a simple exposure metric of "exposed to a gas appliance" does not capture potential variation in the nature or intensity of the exposure, which may vary with frequency of use, intensity of use, use of extractor fans, household ventilation, the proximity to the appliance and the contribution of this source to the individual's total exposure. This may explain the heterogeneity in the results of studies. Second, examination of dose–response effects may be difficult as "frequent use" of a gas cooking appliance also implies frequent exposure to a range of other cooking-related pollutants. Third, and related to the previous point, the group selected for comparison should ideally comprise a group that uses electricity. This may be difficult in countries where gas is used almost universally – for example, until more recently in Hong Kong SAR and Italy. In these circumstances, studies often report comparisons of "frequent users" with "less frequent users".

There are many more studies on the association of health with the presence of gas appliances than with measured nitrogen dioxide and they are of varying quality. While cross-sectional studies are of interest in making a causal inference, greater weight would naturally be placed on those that are longitudinal in design. Further, in older children and adults, objective markers of disease such as lung function may be used and these measurements, in well-designed studies, could be argued to provide better evidence for associations than those that are based on self-reported symptoms. However, respiratory disease may occur in the absence of measurable change in lung function parameters.

Health effects: studies measuring acute health effects of exposure to gas appliances. The acute effects of direct exposure to gas combustion have been studied in people's homes. An early pilot study that used this approach reported change in FVC in asthmatic and non-asthmatic women in whom continuous measurements of nitrogen dioxide were made during cooking at home over a five-day period *(190)*. Spirometric measurements were made before, during and after each cooking period. The highest average nitrogen dioxide level reached was about 1500 $\mu g/m^3$ (0.8 ppm) and the highest five-minute average level was about 1692 $\mu g/m^3$ (0.9 ppm). No formal statistical analyses were presented but in the asth-

matic women, decrements in FVC were seen when cooking with gas on many of the cooking occasions, and when nitrogen dioxide levels reached over 564 μg/m^3 (mean or five-minute average) nearly all asthmatic women showed a drop in FVC. This was not seen in the non-asthmatic women, but it should be noted that the peak nitrogen dioxide levels for the non-asthmatic group were not as high (no reason was given for this). The magnitude of the change in FVC reported in the asthmatic women was substantial, some individuals showing a 10% change in FVC and one individual on one occasion showing a change of 20%.

In another study, 16 adult non-smoking women with asthma had their peak flow measured before and after cooking with gas in their own homes. The fall in peak flow after cooking was related to the level of nitrogen dioxide recorded during cooking (highest peak exposure 500 μg/m^3) and over a two-week period their personal exposure to nitrogen dioxide (range 37.3–135.6 μg/m^3; mean 80.49 μg/m^3) was associated with increased use of salbutamol *(191)*.

Health effects in children: cross-sectional studies looking at exposure to gas appliances. Cross-sectional studies conducted more than 25 years ago suggested that the use of gas cooking was associated with increased hospital admissions for respiratory disease in preschool children in the United States *(179)* and more respiratory symptoms in schoolchildren in England *(174)* and the United States *(192–194)*. Participants in the United Kingdom study were followed for about five years and there was some evidence that the association became less apparent as the children became older *(177)*. Other cross-sectional studies conducted at a similar time did not observe these associations *(180,182,195)* and a longitudinal study in which children were studied for one year to identify episodes of respiratory illness also found no association *(181)*. Many, but not all, of these early studies made attempts to adjust for potential confounding by social class, parental smoking and other household factors, recognizing that the use of gas appliances, in some communities at least, was strongly related to lower socioeconomic status and increased rates of parental smoking *(179)*.

In cross-sectional studies conducted more than 25 years ago, non-significant ($P > 0.05$) decrements in $FEV_{0.75}$ were reported in children living in homes that cooked with gas *(193)*. Hosein et al. *(196)* reported decrements in FEV_1 with the use of a gas stove in 1357 children living in the United States, but this study collected information on eight household factors (pet keeping, hobbies that exposed residents to gases/vapours/dust, cooking fuels, heating system, presence of a fireplace, use of humidifiers or air conditioning, domestic crowding and smokers in the household) and there were significant interactions between some of them, making the overall effect of gas stoves difficult to interpret. Ekwo et al. *(179)* administered isoprenaline to children and examined differences in response in children with different household exposures. Greater bronchodilator responses were observed in children exposed to tobacco smoke than in those who were not

exposed, but no such difference was seen in children exposed to gas cooking appliances, even though an association of symptoms with the use of gas had been observed.

In the past, unvented gas water heaters were relatively common indoor gas appliances in the Netherlands, and researchers have examined their effect on children's health. Lung function was measured by spirometry and a forced oscillation technique in 470 primary school children *(197)*. Respiratory symptoms were non-significantly ($P > 0.05$) more common in children living in homes with unvented gas water heaters. There was no clear, consistent association of spirometric indices or of measurements of impedance with the use of these appliances, although the small observed differences were in the expected direction and were greater for measurements of resistance and impedance in girls.

Large-scale cross-sectional studies have been conducted more recently. In Canadian schoolchildren (n = 10 819), the presence of a gas cooking stove in the home was associated with current asthma (OR 1.95; 95% CI 1.4– 2.68) but not with "wheezing syndrome" after adjustment for a variety of household (e.g. damp, environmental tobacco smoke) and socioeconomic (parental education) confounders *(198)*. A study in eastern Germany conducted in 1992/1993 showed an increased risk of "cough without a cold" (OR 1.63; 95% CI 1.23–2.04) and other cough symptoms in over 2000 children aged 5–14 years living in homes with a gas cooker *(199)*. The lifetime prevalence of other symptoms was not increased. White blood cell counts were increased in children in homes with gas cookers, particularly in those likely to be exposed to high levels of gas-cooking-derived pollutants (those in homes with no extraction fans or smaller homes, and children who spent more time indoors). There was a suggestion that this latter association may be stronger for bottled gas than for the town gas that was in use at the time. In 4–5-year-old Australian children, the use of a natural gas stove was associated with an increased risk of wheeze, asthma and colds *(200)*. In the Third National Health and Nutrition Examination Survey, use of a gas stove for cooking or for heating was associated with an increased risk (OR 1.8; 95% CI 1.02–3.20) of physician-diagnosed asthma in children under the age of six years *(201)*. However, in a large (n ~ 28 700) study of children aged 6–9 years living in Austria and taking part in the International Study of Asthma and Allergies in Childhood (ISAAC, Phase 1), the 12-month period prevalence of wheeze was not associated with gas cooking, although associations with other indoor risk factors such as environmental tobacco smoke, dampness and mould were seen *(202)*.

Effect modification by allergic predisposition, as shown by total IgE levels, on the association of lung function with exposure to gas has been observed in a cross-sectional study of adolescents. Corbo et al. *(203)* studied teenagers in Italy, where the use of gas for cooking is almost universal, and asked them how much time they spent in the kitchen. More girls than boys reported they were "often in the kitchen while their mother cooked" and in girls but not boys those who

reported being "often in the kitchen" had worse lung function as measured by forced expiratory flow rate than those who were in the kitchen only "some of the time". This association was observed mainly in girls with total IgE above 48.6 IU/ml (the median value in girls), suggesting the effect may be greater in girls who are atopic. Effect modification by total IgE level persisted even if children with positive skin tests were excluded. This study suggests a dose-dependent association of exposure to gas cooking with airway function that is modified by both atopy and gender in this age group. It also suggests that proximity to the gas cooker at the time of its use rather than "living in a home with a gas cooker" is the exposure associated with symptoms. However, confounding by exposure to cooking fumes or other pollutants from gas combustion cannot be ruled out.

An analysis of information collected from asthmatic children taking part in the National Health and Nutrition Examination Survey showed that girls who lived in a home with a gas stove (about 45% of the sample) had lower lung function (FEV_1, FEF_{25-75}, FEV_1/FVC) than those who did not *(204)*. However, this association was only seen in girls who did not take asthma medication and was not seen in boys.

The association of respiratory symptoms with gas for cooking may be modified by levels of outdoor nitrogen dioxide. This was examined in a small study in Hong Kong SAR, where cooking with gas (piped town gas and LPG) is almost universal. Children living in two contrasting areas were examined *(205)*. In an area with relatively low background pollution (nitrogen dioxide annual mean 45 $\mu g/m^3$), current doctor-diagnosed "respiratory illness" was more common in children living in homes that cooked most frequently with gas. This dose–response relationship to gas cooking was not observed in a nearby area with higher outdoor background levels of particulate matter and oxides of nitrogen (nitrogen dioxide annual mean 59 $\mu g/m^3$), suggesting that in multicentre studies the association of gas cooking with symptoms may vary with level of ambient pollutants.

Using a case-control design, the association of severe asthma (children whose parents reported that they suffered either 12 or more wheezing attacks in the past 12 months or an attack of wheeze over the same period that limited speech to only one or two words at a time between breaths) with use of gas for cooking was examined *(206)*. Controls were children with no history of asthma or wheezing at any age. There was no evidence that the use of gas for cooking differed between cases and controls (adjusted OR 0.86; 95% CI 0.61–1.23).

Health effects in children: longitudinal studies looking at exposure to gas appliances. A longitudinal study design has been adopted in some studies to examine the health effects of exposure to gas appliances in infancy. Primigravida mothers were interviewed early in pregnancy regarding household characteristics, and the health visitor information on their offspring (n = 1565) was collected at one year of age *(178)*. Although the proportion of children with a respiratory illness

and with an admission to hospital for respiratory illness was higher in homes with gas cooking, the difference was not significant.

The association of exposure to gas appliances in infancy to later respiratory health was examined in Australia, where gas heaters are the main source of indoor combustion products. As part of the Tasmanian Infant Health Survey, the type of heating appliance in use in infancy was recorded and, at the age of seven years, information on respiratory symptoms was collected *(207)*. Only a small proportion of the children lived in homes with a gas heater (most likely to have been fuelled by LPG) but this small group had a substantially increased risk of asthma in later life (1.92; 95% CI 1.33–2.76), even after adjustment for some markers of socioeconomic status (maternal education) and household smoking. In the same publication, the authors presented results from an extended analysis involving more than 6000 children, in which they noted a cross-sectional association of recent wheeze (OR 1.41; 95% CI 1.17–1.71) and asthma (OR 1.33; 95% CI 1.12–1.57) with current use of gas heaters.

Another publication using data from the same children looked at the association of gas use in infancy with lung function *(208)*. Those who had lived in a home with either a gas heater or a gas cooker in infancy were more likely to be sensitized to house dust mites and had a lower $FEV_{1.}$ In the children included in this analysis, the association of asthma with the use of gas was below conventional levels of significance. However, airway obstruction was more strongly associated with current gas cooking in children sensitized to house dust mites than in those not sensitized.

The long-term health effects of exposure to gas appliances was also examined in a United Kingdom study that measured prevalence of wheeze in teenagers in relation to exposure to gas cookers as a child *(209)*. Almost 2000 children provided information on symptoms at ages 7–8 and 15–17 years and, in addition, at the age of 16–18 years reported their use of gas appliances (for cooking or heating) in their current home and in their home when they were a child. Childhood wheezing was associated with childhood exposure to any gas appliance and with childhood exposure to a gas hob (OR 1.47; 95% CI 1.05–2.04). However, childhood exposure to gas appliances was not associated with wheeze that persisted into the teenage years. Wheeze in adolescence was not associated with current teenage exposure and, surprisingly, persistent wheeze was less frequent in those exposed to gas in the teenage years. The authors argued that this latter observation might be explained by selective avoidance.

A similar age group was studied as part of a longitudinal study in southern California *(210)*. Participants aged 9–16 years were recruited and followed for five years or until graduation. Excluding those with "ever physician-diagnosed asthma" at baseline, the association of indoor factors with doctor-diagnosed asthma was examined in the remaining 3535 children. In this group, at baseline, the use of gas for heating and for cooking was common and more commonly

reported by those who had wheeze (78% of those with wheeze and 73.8% of those without wheeze used gas for heating ($P = 0.004$), while 79.4% of those with wheeze and 77.7% of those without wheeze had a gas stove ($P = 0.27$)). Over the five-year period, there was no evidence that the presence of these appliances was associated with the incidence of physician-diagnosed asthma in children with or without wheeze at baseline.

Longitudinal studies have been used to examine whether exposure to gas appliances has a deleterious effect on lung growth in children. In Arizona, United States, a four-year study was conducted to determine whether living in a home where gas was used for cooking was associated with poor lung growth in children aged eight years at baseline. Despite strong cross-sectional associations of the use of gas for cooking with symptoms of wheeze, cough and sputum production at baseline, there was no evidence that exposed children had lower rates of lung growth than unexposed children *(192)*.

These findings are supported by work conducted as part of the Six Cities Study in the United States. First reports from the study suggested that exposure to gas stoves was associated with reduced lung function in children *(194)*. Later work suggested that a reduction of 0.7% in mean FEV_1 and 0.6% in mean FVC seen in the first examination was not observed after three years of follow-up, where a non-significant reduction of 0.3% in both measurements was seen *(182)*. After further examination, analyses based on 7834 children aged between six and ten years who had between two and five annual measurements of lung function showed no effect of the use of a gas stove on pulmonary function level at the end of the study *(211)*.

As part of the meta-analysis conducted by Hasselblad et al. *(170)* in the early 1980s, the association of childhood respiratory illness with the use of gas for cooking was determined to be 1.15 (95% CI 1.09–1.22).

Health effects in adults: cross-sectional studies looking at exposure to gas appliances. If we hypothesize that the health effects of combustion products such as nitrogen dioxide from unvented gas appliances depend on repeated high exposures, those that actually use the appliances and are therefore exposed to these peaks would be expected to be at greatest risk. In most communities, cooking remains a task largely performed by women and particularly by young and middle-aged women with large families. This being so, we might expect women to be at particular risk. However, one of the first studies examining the association of the use of gas with respiratory health suggested the opposite. In a community-based representative sample of almost 2000 adults in Maryland, United States, men living in homes with a gas cooker had more chronic cough and wheeze with breathlessness than those living in homes with electric cookers. No association was seen in women. The authors hypothesized that women have, over thousands of years, been exposed to pollutants generated by cooking and heating and have

an evolutionary advantage over men in being resistant to the health effects of exposure to fumes from cooking and cooking appliances *(212,213)*.

A small case-control study was conducted shortly afterwards. The type of cooker that was used by 102 non-smokers with FEV_1 in the highest quartile of the distribution was compared with that used by 103 non-smoking women with FEV_1 in the lowest quartile *(214)*. Exposure to gas appliances was non-significantly higher in those with low lung function (30.4% vs 22.3%; OR 1.82; P = 0.076) and cooking with gas for more than 10 years was more common in those with low lung function. Effect modification by atopy or frequency of use was not examined.

Large-scale cross-sectional studies conducted more recently in the United States suggest little association of symptoms with use of gas in either men or women. For example, in the National Health and Nutrition Examination Survey III (NHANES III), the association with gas stove use was examined in 7630 lifelong non-smokers (mean age 42 years) *(215)*. There was no association of current gas stove use with symptoms of phlegm, wheeze or dyspnoea, although an association with chronic cough was seen (OR 1.6; 95% CI 1.1–2.3). In fact, those who had a gas stove appeared to have *better* lung function than those who did not. These analyses were extensively adjusted for other household and sociodemographic factors. Effect modification by gender (and by atopy as measured by skin tests) was tested and was not observed.

Nevertheless, an analysis of data collected as part of the ECRHS multicentre study presented evidence that respiratory symptoms suggestive of asthma, and lung function changes suggestive of airway obstruction, may be associated with the use of gas cooking in some communities *(216,217)*. A strong cross-sectional association of respiratory symptoms with the use of gas for cooking was seen in women, but not men, living in three towns in England. The association was particularly strong in women (P for interaction < 0.05). Women who were sensitized to one of four common aero-allergens were particularly at risk, although formal tests for effect modification by atopy in women were not significant (P for interaction > 0.05). These observations were supported by decrements in FEV_1 and FEV_1/FVC. As part of the ECRHS, the same protocol was followed in other research centres in Europe. However, when the same statistical approach was extended to include these centres, considerable heterogeneity was observed between centres with the strongest effects being seen in the United Kingdom centres. No explanation for this heterogeneity was found but it may have been due to the varying exposure suggested by reporting that a participant "mainly uses gas for cooking". In this early study no information on frequency of use, use of natural ventilation, type of gas used and maintenance of appliances was collected.

Researchers in the Netherlands *(218)* looked for effect modification by atopy on the association of gas cooking with bronchial reactivity. The protocol adopted for the study was that of the ECRHS but the age range studied was larger (20–70

years). Atopy was defined by the presence of specific IgE to common aero-allergens and measured bronchial reactivity to methacholine. There was no evidence that atopics had greater bronchial reactivity if they used gas for cooking, but the associations were much stronger in both men and women who had high total IgE compared to those with low total IgE. The authors argued that total IgE was a superior way of identifying the susceptible "atopic" subgroups but to date their findings have been supported only by the study of adolescents in Italy *(203)*. Total IgE is higher in smokers *(219)* and in those exposed to "gas, dust, fumes or mists" in the workplace *(220)*. None of these authors considered whether total IgE was higher in those who cooked with gas and was a surrogate marker for greater exposure to gas.

Older adults may not use their gas cooking appliances as frequently as those living with small children. In a questionnaire survey of men and women aged 65 years or older in Bristol, United Kingdom, the presence of a gas hob or gas oven was associated with a small, non-significant risk of respiratory symptoms suggestive of COPD *(221)*. The risk of respiratory symptoms appeared to be higher in women than in men for gas hobs, although the gender interaction was not significant ($P > 0.05$). Many people in this age group will no longer be preparing meals for their families and no information was collected on the frequency of use of gas hobs and ovens. Associations may have been weak owing to infrequent cooking in this age group.

Many of the remaining cross-sectional studies in adults have been restricted to women. In Polish women over 65 years of age, chronic cough, chronic phlegm and shortness of breath on exertion were more common in those who cooked with gas for more than three hours a day compared to those who cooked with gas less frequently *(222)*. The authors reported that "decline in FEV_1" was also greater in this group, but this association was assessed by comparison of the age coefficient for regression equations of FEV_1 on height and age, stratified by those with short or medium/long daily exposure, and was not derived from repeated measurements of FEV_1 .

In a study of 1282 women in Singapore (223), there was a non-significant increased risk of respiratory symptoms among non-smoking women who cooked frequently and a significantly reduced adjusted FEV_1 noted in those who described themselves as housewives and who cooked frequently (0–2 times a week 1.82 litres; 3–14 times a week 1.62 litres; ≥ 15 times a week 1.61 litres). In Singapore, as in Poland, the use of gas for cooking was universal and greater exposure to "cooking with gas" also implies greater exposure to other substances generated by the cooking process. Stir frying with spices and chillies is a common method of cooking, and regular cooking is most likely to be associated with greater exposure to oil mists and frying fumes that may themselves cause respiratory symptoms. There was a strong association of chronic cough and phlegm with the frequency with which the kitchen was "filled with cooking fumes". This could

reflect poor ventilation and greater exposure to the products of gas combustion, but could also reflect greater exposure to pollutants created by cooking.

A cross-sectional study of asthmatics recruited into NHANES III *(215)* did not show an association of the use of gas cooking with asthma severity. Nearly half of the 445 asthmatics studied cooked with gas but they had only a non-significant increased prevalence of symptoms of wheeze and dyspnoea and had the same lung function (FEV_1, FVC or $FEF_{25–75}$) as those who cooked with electricity. The authors of this study concluded that their results "should be reassuring to adults with asthma and their health care providers". In another report, the same research group followed asthmatics living in California over an 18-month period. Those who cooked with gas had similar health service utilization rates (hospital admissions and emergency department visits) as those who cooked with electricity. There was no evidence that the reporting of use of a gas stove at baseline (or changing the use of that gas stove over the period of the follow-up) was associated with asthma severity or with SF-12 or asthma-specific quality of life scores, even though associations with exposure to ETS were observed *(224)*.

Health effects in adults: longitudinal studies looking at exposure to gas appliances. Longitudinal studies over several years of follow-up to examine the chronic respiratory health effects of gas cooking in adults are less common than cross-sectional studies, but some have been published. Keller et al. *(180)* examined incident lower respiratory illness in members of 441 families living in Ohio, United States by contacting the families every two weeks over a period of a year. About half of the families used electricity to cook and the rest used gas, but overall the rates of respiratory illness in mothers (and children) were lower in families with gas cookers than in families with electric cookers.

The longest follow-up has been of residents of households in Chesterfield, England, that were included in a housing survey in 1936. They were followed through the National Health Service Central Registry *(225)*. The presence of a gas cooker in the home at the time of the survey was not associated with overall mortality in children or adults and was negatively associated with death ascribed to COPD (RR 0.8; 95% CI 0.6–1.2). This result is unsurprising, as positive results would have implied a very strong association of gas cooking at one point early in life with development of severe respiratory disease many years later, without adjustment for smoking.

The largest longitudinal study with the most comprehensive analysis to examine respiratory outcomes in adults, based on exposures in earlier life, was from the 1958 birth cohort in the United Kingdom *(226)*. In a sample of 1500 adults enriched with people who had a history of wheezing in earlier assessments, information on the fuel currently used for cooking and the fuel used for cooking when the participant was 11 years old was collected at age 35 years. Of those who first reported symptoms indicative of asthma at the age of 7 years, those

who reported using gas for cooking at age 35 years were more likely to report current wheeze than those who currently used electricity for cooking (OR 1.26; 95% CI 0.84–1.88). This increased risk was greater in women (OR 1.82; 95% CI 1.02–3.26) than in men (OR 0.86; 95% CI 0.48–1.58) and in non-atopics (OR 1.84; 95% CI 1.05– 3.22) than in atopics (OR 0.76; 95% CI 0.39–1.49), but the interaction of gender and atopy with gas cooking for persistence of symptoms was not significant ($P > 0.05$). Cross-sectional analyses of the 243 people with asthma or wheeze in the previous year showed little evidence that the current use of gas for cooking was associated with current asthma severity as measured by number of attacks of asthma or the reporting of sleep disturbed by wheezing in the previous 12 months.

At variance with the results for symptoms is that decrements in lung function were associated with the use of gas for cooking in men (FEV_1 –141 ml; 95% CI –234 to –48 ml) but not in women, and current asthmatics showed worse lung function if they cooked with gas than if they cooked with electricity (FEV_1 –129 ml; 95% CI –234 to –14 ml). This latter association was not examined in men and women separately. The authors concluded that "past and current use of gas for cooking is unlikely to be a major influence on respiratory morbidity in young adults".

A longitudinal design was used to assess acute health effects of exposure to gas appliances in a panel study of 164 asthmatics living in Denver, United States *(227)*. Participants recorded symptoms, medication use and their use of indoor gas appliances. The reporting of moderate or severe cough and shortness of breath was associated with gas stove use on that day, the "non-users" comprising people with either a gas or an electric stove.

Studies conducted in developing countries

In developing countries, many people cook with either biomass or with gas (usually LPG). Use of biomass is associated with a range of health effects, which were reviewed in 2004 *(228)*. Solid fuel use was shown to be associated with acute lower respiratory tract infection, COPD, asthma, cataracts, tuberculosis and lung cancer. Association of nitrogen dioxide with disease in these settings is likely to be confounded by the high particulate counts. There has, however, been one study in Ethiopia where about 90% of homes cook with biomass (wood or charcoal) and the remainder cook with a modern fuel such as kerosene, gas or electricity *(229)*. Those who used kerosene had a significantly increased risk of IgE sensitization to aero-allergens, eczema and rhinitis compared to those who did not. Those who used gas had some increased risk and those who used electricity had an increased risk for eczema only. The authors argued that the increased risk of allergic outcomes in those using modern fuels producing nitrogen dioxide was unlikely to be explained by factors associated with socioeconomic status, as they had adjusted for this (family occupation, household crowding).

Health effects: type of gas

Some of the variation in the associations of gas cooking with symptoms may be explained by the type of gas used. In areas where there is no piped gas, LPG is often used. In a study of more than 25 000 children in the United Kingdom, there was no association of gas used for cooking or heating with wheeze symptoms *(230)*. Children who lived in homes that used bottled gas (which in this study also included paraffin) were at an increased risk of wheeze compared to those using electricity for heating (OR for speech-limiting wheeze 1.38). One of the few studies in developed countries to examine the association of bottled gas compared to mains gas on respiratory health in adults was conducted in Italy, where cooking with gas is almost universal. In a population-based study in the Po Delta *(231,232)*, 30% of people used bottled gas and 67% used natural gas for cooking. The type of gas used for cooking was closely associated with the type of heating in the home, and exposure status was defined by both heating and cooking appliances. The lowest prevalence of symptoms was in those with natural gas central heating and gas cooking. Dyspnoea was more common in men and women who used bottled gas for cooking compared to those who used natural gas. No effect modification by atopy was examined or reported. Viegi et al. *(231)* hypothesized that the use of bottled gas may produce more pollutants from gas combustion owing to inefficient burning that went unnoticed. Bottled gas appliances were not subject to the mandatory regulation and official inspection imposed on natural gas appliances.

Health effects: studies conducted in ice arenas

High concentrations of nitrogen dioxide are observed in indoor ice arenas that use resurfacing machines powered by combustion engines, and studies have been conducted to assess the effect of exposure to nitrogen dioxide in this setting. A review of studies in which measurements were made of both nitrogen dioxide and carbon monoxide in indoor ice arenas was published in 2002 *(233)*. Exposure to nitrogen dioxide in this setting is accompanied by exposure not only to carbon monoxide and particles but also to cold air, and cross-sectional studies suggesting a high prevalence of respiratory symptoms in ice hockey players and figure skaters *(234)* may reflect a response to cold air. This interpretation is supported by evidence that the prevalence of asthma is higher in those who participate in outdoor winter sports such as cross-country skiing *(235)*.

To overcome this problem, one study in Sweden compared respiratory symptoms in children who played ice hockey in ice arenas with propane-fuelled and electric resurfacing machines *(236)*. Some 1500 children aged between 10 and 16 years who had played ice hockey in the previous three years and had trained in one of 15 indoor ice arenas were identified. Nine of the arenas used a propane-fuelled resurfacing machine and the median nitrogen dioxide level obtained from three consecutive days of monitoring in each arena during opening hours was 190

μg/m^3, although there was considerable range in the daily measurements (28–1016 μg/m^3). The remaining six arenas used electric resurfacing and the equivalent indoor nitrogen dioxide levels were 9 μg/m^3 (4–31 μg/m^3). Symptom prevalence (wheezing in the last 12 months, exercise-induced wheeze, physician-diagnosed asthma or current rhinitis) was non-significantly higher in children who trained in arenas with an electric resurfacing unit rather than a propane unit. The authors then looked at children attending the propane arenas only. They considered exposure as "high nitrogen dioxide" if levels were above the median and low if below the median. All symptoms were more common in those attending high nitrogen dioxide propane arenas and this reached statistical significance for those who had ever had symptoms of rhinitis (OR 1.7; 95% CI 1.3–2.3), rhinitis in the last 12 months (OR 1.7; 95% CI 1.2–2.4) and those who had ever had wheezing (OR 1.4; 95% CI 1.0–1.9). The vast majority of the children (over 80%) had played ice hockey for more than three years in these arenas.

Chronic health effects of exposure were also examined in Finland *(43)*. Junior ice hockey players were asked to complete a questionnaire. Information on the weekly average nitrogen dioxide in the ice arenas in which they trained was collected (range 21–1176 μg/m^3; mean 228 μg/m^3). For each increase of 100 μg/m^3, the risk of reporting rhinitis and cough was significantly increased (OR 1.54; 95% CI 1.05–2.26 for rhinitis and OR 1.62; 95% CI 1.06–2.47 for cough) and that of mucus production and sore throat was non-significantly increased (OR 1.41; 95% CI 0.96–2.08 for mucus production and OR 1.43; 95% CI 0.88–2.35 for sore throat), although in the discussion the authors intimate that the relationship is non-linear.

There are case reports of acute pneumonitis in adult ice hockey players in the 24 hours after a match *(237,238)*, but these studies lacked indoor nitrogen dioxide measurements. However, as part of an investigation into acute onset of cough, haemoptysis and/or chest pain during or shortly after playing hockey in an indoor ice arena among the members of four ice hockey teams *(239)*, the mean nitrogen dioxide level during 30 minutes of resurfacing was found to be 7520 μg/m^3. In 1994, a similar incident occurred in Stockholm, Sweden, probably associated with exposures of up to 2358 μg/m^3 *(240)*, and five years later the prevalence of self-reported shortness of breath, wheezing, cough and rhinitis was higher in those exposed to the high levels of nitrogen dioxide than in the control group (ice hockey players who had trained in electric resurfacing arenas) *(241)*. Longer-term health effects of high-dose exposures were also reported from Philadephia, United States *(242)*. Six months after an incident in which 16 previously healthy hockey players developed symptoms following exposures thought to be between 658 and 2068 μg/m^3 for around 3 hours, 50% remained symptomatic. Impulse oscillometry tests before and after bronchodilator use suggested increased airway resistance and small airway disease in those reporting more symptoms.

Nitrous acid

Nitrous acid is present as a gas in indoor and outdoor air. In the indoor environment it is produced both directly by combustion processes, such as by the use of unvented gas appliances, and indirectly by absorption of nitrogen dioxide and then release of nitrous acid from water-containing surfaces in the home *(243)*. One chamber study in healthy volunteers showed that exercising in 650 ppb nitrous acid for three hours is followed by minor reductions in airway conductance *(244)* and another small study in asthmatics, again conducted in a chamber, showed that similar levels of exposure are associated with minor reductions in forced vital capacity *(245)*.

It has been established that the presence of nitrous acid will interfere with accurate measurement of nitrogen dioxide by most commonly used methods, and it has been proposed that adverse health outcomes that have been attributed to nitrogen dioxide (or to exposure to appliances producing nitrogen dioxide, such as gas stoves) could be confounded (or explained) by exposure to nitrous acid *(243,246)*. It has been argued that the variations in the reported association of indoor nitrogen dioxide with respiratory health may be explained by failure to measure this co-pollutant *(247)*. The dearth of studies in which both have been measured has been identified as a gap in our understanding of the health effects of gas appliances *(247)*.

In a study of infants at high risk of developing asthma because they had an older sibling with physician-diagnosed asthma, both indoor nitrous acid and nitrogen dioxide were measured and lung function assessed *(40)*. As referred to earlier in this chapter, the authors concluded that nitrogen dioxide, not nitrous acid, was more closely associated with lower lung function. Nevertheless, in a small study of British adults, decrements in lung function were associated with exposure to nitrous acid in the kitchen (predicted decrease in FEV_1 0.96% (95% CI 0.09–1.82) and decrease in FEV_1/FVC 0.45% (95% CI 0.06–0.83) per 1-ppb increase in indoor nitrous acid) and the association persisted after adjustment for nitrogen dioxide *(248)*.

Health risk evaluation

The main health outcomes of interest are respiratory symptoms, bronchoconstriction, increased bronchial reactivity, airway inflammation, and decreases in immune defence leading to increased susceptibility to respiratory infection. No other health effects have been consistently associated with exposure to nitrogen dioxide in the indoor environment.

Quality of exposure and effect assessment

Controlled exposure studies in humans that assess the health effects of short-term exposures give no cause for concern regarding exposure assignment/measurement. In epidemiological studies, exposure assignment is less precise, being

based on passive samplers (which provide average levels over several hours or weeks) or on proxy measurements (e.g. the presence of a gas appliance). The latter is an imprecise estimate of actual exposure but, at group level, is associated with elevated long-term indoor exposure to nitrogen dioxide and with short-term peaks of exposure. No biomarker is available.

Controlled exposure studies in humans assessing the health effects of short-term exposures have used well-standardized, objective methods for the assessment of health effects. In epidemiological studies, self- (or maternally) reported symptoms have been widely used as the health metric. These measurements are susceptible to over-reporting by those who perceive their exposure to be high. Although lung function measures provide more objective estimates of health status, inflammatory changes and symptoms may occur in the absence of lung function changes.

Controlled exposure studies in humans have shown acute respiratory health effects of short-term exposures in healthy volunteers or those with mild pre-existing lung disease. Mechanical failure of resurfacing machines in ice arenas leading to short-term, high-dose exposures demonstrates similar effects and suggests there may be long-term sequelae. Population-based studies have shown health effects of chronic indoor nitrogen dioxide exposure in infants, children and adults.

Levels and duration of exposure

Controlled exposure studies in humans have assessed acute health effects to short-term exposure (maximum of several hours) at levels consistent with peak exposures experienced when gas appliances are used, but well above the average levels in most indoor environments. The majority of epidemiological studies have examined populations with average indoor levels that can be considered representative of longer-term population exposures.

Exposure–response relationship

There is evidence of a dose–response effect in controlled exposure studies (particularly at high levels) and in epidemiological studies. There is no evidence for a threshold in epidemiological studies. The exposure–response effect of repeated daily peak exposures to nitrogen dioxide is not known.

Susceptible population or response modifiers to consider in guideline setting

Controlled exposure studies assessing the health effects of short-term exposures show health effects at lower levels more consistently in asthmatics than in non-asthmatics, and both chamber studies and some epidemiological studies suggest that exposure enhances the response to allergens in those who are sensitized. Some epidemiological studies suggest stronger associations of respiratory health

with indoor nitrogen dioxide in females compared to males, but it is not clear whether this is due to women spending more time indoors or an underlying biological basis.

Quality of evidence

Although associations of exposure with health are well-documented, there is unexplained heterogeneity in results from well-conducted studies. This may reflect underlying variations in the nature of the exposure or in host susceptibility.

There is sufficient evidence of a causal relationship between controlled exposure to nitrogen dioxide concentrations as low as 380–560 μg/m^3 for periods of one hour or longer and a range of responses within the lung that suggest airway inflammation and alteration in lung immune defences in asthmatics. Recent systematic review and meta-analysis provides suggestive evidence that controlled exposures to as low as 188–360 μg/m^3 are associated with small increases in airway reactivity to a range of stimuli in asthmatics. Studies that have examined health effects of repeated short exposures to 500 μg/m^3 provide suggestive evidence that this is associated with exaggerated/prolonged response to allergen challenge in asthmatics/atopics. There is limited or suggestive evidence of an association between indoor nitrogen dioxide at levels currently occurring in populations and (*a*) reported respiratory symptoms in children, (*b*) increased reporting of symptoms in children with asthma, (*c*) increased asthma severity following respiratory viral infection and (*d*) reported respiratory symptoms in adults.

Health relevance of current indoor exposures in various regions of the world

Epidemiological studies conducted in several countries show that a proportion of homes and classrooms have indoor nitrogen dioxide levels exceeding the WHO ambient guidelines for outdoor air.

Indoor studies suggest that those using gas cookers, particularly in poorly ventilated spaces, can experience peak nitrogen dioxide exposures in excess of 500 μg/m^3. Important factors that may increase indoor exposure are the use of unvented gas appliances, poor ventilation, proximity to major highways and the use of propane- and petrol-fuelled ice resurfacing machines in indoor ice arenas.

Guidelines

A 1-hour indoor nitrogen dioxide guideline of 200 μg/m^3, consistent with the existing WHO air quality guideline, is recommended.

At about twice this level, asthmatics exhibit small pulmonary function decrements. Those who are sensitized may have small changes in airway responsiveness to a variety of stimuli already at this level. Studies of the indoor environment provide no evidence for an indoor guideline different to the ambient guideline.

An annual average indoor nitrogen dioxide guideline of 40 μg/m^3, consistent with the existing WHO air quality guideline, is recommended.

The ambient annual average guideline of 40 μg/m^3 was initially based on a meta-analysis of indoor studies. It was assumed that having a gas stove was equivalent to an increased average indoor level of 28 μg/m^3 compared to homes with electric stoves, and the meta-analysis showed that an increase in indoor nitrogen dioxide of 28 μg/m^3 was associated with a 20% increased risk of lower respiratory illness in children. Homes with no indoor sources were estimated to have an average level of 15 μg/m^3. Several exhaustive reviews to further develop ambient guidelines have not challenged these findings.

Recent well-conducted epidemiological studies that have used measured indoor nitrogen dioxide levels support the occurrence of respiratory health effects at the level of the guideline.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome(s) for guideline definition

Respiratory symptoms, bronchoconstriction, increased bronchial reactivity, airway inflammation and decreases in immune defence, leading to increased susceptibility to respiratory infection.

Source of exposure–effect evidence

- Short-term exposures: human controlled exposure experimental studies indicating minor changes in pulmonary function in people with asthma exposed to 560 μg/m^3 nitrogen dioxide for up to 2½ hours *(124–126)*. Small increases in airway reactivity to a range of stimuli in asthmatics at repeated short exposures to 500 μg/m^3 *(131,133,136,137)*.
- Long-term exposures: meta-analysis of studies on association of lower respiratory illness in children showing that an increase in indoor nitrogen dioxide of 28 μg/m^3 above the background of ca. 15 μg/m^3 was associated with a 20% increased risk of lower respiratory illness in children *(170)*.

Supporting evidence

- Significant association of various respiratory symptoms or lung function indices with nitrogen dioxide measured indoors or as personal exposure in all identified epidemiological studies of asthmatics *(23,26,160–162,164,165,168,191,268)*. Lowest measured levels were ca. 5 μg/m^3.
- Associations also found in half of the studies of non-asthmatic children *(10,27,40,146,147,148,153,154,156,158,208)*.

Results of other reviews

WHO *Air quality guidelines: global update 2005 (15)* and EC INDEX project *(5)* agreed on the same set of guidelines.

Guidelines

– 200 μg/m^3 – 1 hour average.
– 40 μg/m^3 – annual average.

Comments

No evidence from epidemiological studies for an exposure threshold.

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Table 5.1. Levels of nitrogen dioxide in various countries

Reference	Project / programme	Country	Averaging time / survey year(s) / methods	Location of measurement
Baxter et al. *(24,25)*		United States (Boston, MA)	3–4 days from 2003 to 2005 in 2 seasons (May–October, December–March)	
Belanger et al. *(164)*		United States	Palmes tubes	
Berglund et al. *(249)*	INDEX	Sweden	24 hours Urban area Rural area	Schoolchildren, personal exposure
Bernard et al. *(250)*		France	14 days (passive monitors)	
Blondeau et al. *(21)*	PRIMEQUAL	France (La Rochelle)	2 weeks	
Brauer et al. *(251)*	International survey NO_2 indoor ice skating	9 countries	1 week average	
Breysse et al. *(252)*		United States (Baltimore, MD)	72 hours	
Chao *(253)*		China (Hong Kong SAR)		
Cyrys et al. *(254)*	THADE	Germany (Hamburg) Germany (Erfurt)	1 week mean	Living room
Diette et al. *(163)*		United States (East Baltimore, MD)	72 hours	Bedroom
Dutton et al. *(33)*		United States (Boulder, CO)	4 hours in 1999	
Emenius et al. *(143)*	BAMSE birth cohort	Sweden (northwest Stockholm): Urban area Semi-urban area Suburban area	4 weeks (passive samplers)	Living room
Franklin et al. *(37)*		Australia	During summer (passive samplers)	Kitchen

Emission source	Number of homes / volunteers	NO_2 measurement results ($\mu g/m^3$) [a]	Comments
	43	37.5 (mean)	Low socioeconomic status households (I/O ratio 0.99 +/– 0.63)
Electric stoves	728 children	16.45 (SD 17.41)	
Gas stoves		49.55 (SD 34.62)	
		13 (median) 7 (median)	Most important source of exposure = indoor ice skating (levels up to 8000 $\mu g/m^3$)
	107 volunteers	31.9 (mean) / 12.7 (SD)	Personal exposure
	8 schools		I/O ratio 0.88–1
Type of fuel used in the resurfacing machine	332 ice arenas	436.16 (AM) (breathing height to the ice surface); 422.77 (spectators' area)	
	100 (bedroom)	60.45 / 76.9 (SD)	25% of the samples below the limit of detection
	60 people (personal exposure)	46 (mean) (60 personal exposures)	When cooking 59.7 $\mu g/m^3$; when not cooking 41.8 $\mu g/m^3$
	12 people (homes: living room, bedroom, kitchen)	47.3 (mean) (12 personal exposures; 55.2 (12 indoor measurements)	
	201	17 (median)	
	204	15 (median)	
	300 Inner-city preschool children (150 with asthma, 150 controls)	41.32 (median, children with asthma); 40 (median, controls)	
	2	688.68 (mean)	Measurements during operation of unvented natural gas fireplaces
Few gas combustion appliances	540		Mean outdoor levels:
(8.52% of homes with gas stove)		18.3 (mean) (8 – 45.1) 12.2 (mean) (4.4 – 25.1) 8.1 (mean) (2.3 – 21.1)	31.5 (17.9–46.7) 21.6 (8.7–36.4) 13.7 (6–29)
Gas cooker	53	Average 16.2 (12.7–20.6); peak 45.3 (36–57.1)	

[a] AM = arithmetic mean, SD = standard deviation, GM = geometric mean, max = maximum value.

Reference	Project / programme	Country	Averaging time / survey year(s) / methods	Location of measurement
Gallelli et al. *(255)*	THADE	Italy (Genoa)	2 months in 2000 (passive diffusion tubes)	Kitchen Bedroom
Garcia Algar et al. *(256)*		United Kingdom (Ashford) Spain (Menorca) Spain (Barcelona)	Between 7 & 15 days (passive filter badges)	
Garcia Algar et al. *(13)*		Spain (Barcelona)	Over 7–30 days between 1996 & 1999 (passive filter badges)	
Garrett et al. *(31)*	THADE	Australia (Latrobe Valley, Victoria)	4 days in 1994/1995 (passive samplers)	
Gee et al. *(257)*	THADE	United Kingdom (Manchester)	5 days	Living room Bedroom
Gilbert et al. *(258)*		Canada (Quebec City)	7 days between January & April 2005 (passive monitors)	
Guo et al. *(259)*	INDEX	China (Hong Kong SAR)	15 minutes 15 minutes	Ice skating arenas
Hagenbjork-Gustafsson et al. *(7)*	THADE PEACE	Sweden (Umeå, suburban control)	2 x 24 hours between January & March 1994	
Hazenkamp-von Arx et al. *(16)*	ECRHS II	21 European study centres of ECRHSII (from northern Italy to Iceland)	14 days in 2000 (passive sampler)	
Kattan et al. *(23)*	NCICAS	United States (8 inner city areas)	7 days (Palmes tubes)	Child's sleeping area

Emission source	Number of homes / volunteers	NO_2 measurement results ($\mu g/m^3$) [a]	Comments
	89	47 (indoor mean) 24.78 (indoor mean) 24.9 +/– 7.8 (students, personal exposure); 44.3 +/–10.1 (workers); 40 +/– 13.4 (housewives)	
Gas combustion appliances, cigarette smoking	1421 (living room wall)	11.07 (median) 11.59 (median) 45.66 (median)	
	340	45 (mean in 1996); 53.22 (mean in 1997); 51.69 (mean in 1999)	
Gas stoves, vented gas heaters, smoking	80	11.6 (median, ranging from < 0.7 to 246)	Highest levels recorded in winter
	69	27.2 (AM) 20.3 (AM)	
	96	8.3 (3.3–29.1)	
Gasoline fuelled Propane fuelled		58 – 91 (AM) 242 (AM)	
No gas appliances	23 (urban area) 20 (suburban control area)	11 (mean in urban area) 6 (mean in control area)	I/O ratio: 0.44 I/O ratio: 0.67 Heavier traffic density in Umeå
		Annual mean from 4.9 to 72.1	
Gas stoves	469 (1444 children)	57 (median)	Indoor levels considerably higher than US national outdoor median value (34.43)

[a] AM = arithmetic mean, SD = standard deviation, GM = geometric mean, max = maximum value.

Reference	Project / programme	Country	Averaging time / survey year(s) / methods	Location of measurement
Kousa et al. *(260)*	EXPOLIS	Switzerland (Basel) Finland (Helsinki) Czech Republic (Prague)	48 hours in 1996/1997 (passive samplers)	
Lambert et al. *(11)*	THADE	United States (Albuquerque, NM)	2 weeks mean in 1988–1991 (passive diffusion samplers)	Kitchen Living room Bedroom
Lawrence et al. *(30)*		India (Agra)	October 2002 to February 2003 (multigas monitor)	
Lee & Wang *(41)*	INDEX			Chamber test
Lee et al. *(39)*		United States (2 communities: Upland & San Bernardino County, southern California)	6 days in April & May 1996 (passive samplers)	
Leung et al. *(9)*	THADE	China (Hong Kong SAR)	1 week mean (stationary samplers)	Kitchen Bedroom Lounge
Levy et al. *(3)*	THADE	Finland (Kuopio) Norway (Kjeller) Switzerland (Geneva) Germany 1 (Erfurt) Canada (Ottawa) Germany 2 (Berlin) Croatia (Zagreb) United States (Boston, MA) United Kingdom 3 (London) Japan 2 (Sapporo) Philippines (Manila) China (Beijing) Poland (Sosnowiec) Republic of Korea 1 (Taejon) India (Bombay)	48 hours in 1996	

Emission source	Number of homes / volunteers	NO_2 measurement results ($\mu g/m^3$) [a]	Comments
	262 adults	27/13 (SD in residential indoor) to 36/24 (SD in workplace) 18/11 (SD in residential indoor) to 27/15 (SD in workplace) 43/23 (SD in residential indoor) to 30/18 (SD in workplace)	Mean outdoor levels: 36 +/– 13 24 +/– 12 61 +/– 20
Gas cooking stoves	1205 children / homes	65.04 (AM) 55.48 (AM) 40.17 (AM)	Lower indoor concentration observed during the summer
		487.81/279.3 (SD)	Measurements conducted in rural, urban and roadside
Mosquito coils and candles burning		17–91 (AM)	NO_x most abundant gas pollutants relating to candle burning
	119 homes (57 in Upland, 62 in San Bernardino)	53.56 (mean)	Average indoor NO_2 concentration (38.26 $\mu g/m^3$) was significantly higher than outdoor concentrations
	40 homes	93.16 (AM) 58.1 (AM) 59.6 (AM)	
	30 30 33	10.34 (mean) 14.66 (mean) 15.60 (mean)	
	29 29 31 15 20	16.97 (mean) 20.12 (mean) 23.12 (mean) 31.58 (mean) 36.10 (mean)	
	117	40.42 (mean)	
	59 14	43.43 (mean) 45.12 (mean)	
	44 15	47.75 (mean) 64.67 (mean)	
	40	72.76 (mean)	
	20	76.70 (mean)	

[a] AM = arithmetic mean, SD = standard deviation, GM = geometric mean, max = maximum value.

Reference	Project / programme	Country	Averaging time / survey year(s) / methods	Location of measurement
		Japan 3 (Tokushima) Republic of Korea 2 (Seoul) Mexico (Mexico City)		
Lindgren *(261)*				Cabins
Mi et al. *(262)*		China (Shanghai)	7 days (diffusion samplers)	30 classrooms
Monn et al. *(263)*	THADE SAPALDIA	Switzerland (4 urban, 2 rural & 2 alpine areas)	1 week in 1993/1994 (passive sampler)	Personal exposure
Mosqueron et al. *(264)*		France (Paris)	48 hours (passive samplers)	Personal exposure Living room Indoor office
Nakai et al. *(18)*		Japan (Tokyo)	10 seasons over 3 years (personal exposure)	
Noy et al. *(265)*	INDEX	Netherlands	3 measurements of 1 week within a year (Palmes tubes)	Kitchen
Osman et al. *(187)*		United Kingdom(North East Scotland)	1 week	Living room
Pennanen et al. *(42)*	INDEX	Finland	Max 15 minutes Max 1 hour	Indoor ice arenas
Pennanen et al. *(266)*	INDEX	Finland	1 week	

Emission source	Number of homes / volunteers	NO_2 measurement results ($\mu g/m^3$) [a]	Comments
	30	78.77 (mean)	
	31	81.22 (mean)	
	30	117.88 (mean)	
	26; intercontinental flights (Boeing 767-300)	14.1 (mean) 37 (max)	
	10 naturally ventilated schools	33–85	Outdoor : 45 – 80 $\mu g/m^3$ I/O ratio : 0.63 – 1
Gas cooking Smoking	more than 500 subjects	27 (average personal exposure) 21 (average indoor measurements)	Personal exposure correlated best with indoor; outdoor average 31 $\mu g/m^3$
	62 office workers	43.6 (mean personal exposure) 35.1 (mean in home) 44.9 (mean in office)	
Gas cooking stoves, heaters	50 residents from 3 residential zones A: 0–20 m from the roadside B: 20–150 m from the roadside C: residential district, suburban area	 121.28 (mean) 116.7 (mean) 105.79 (mean)	Outdoor concentrations in zone A were always the greatest
Gas stoves		2500 (max)	
Smoking (39% of the 148 patients)	148 patients (home measurements)	14.92 (mean)	
Ice resurfacing machines with combustion engines		320 – 7530 (max) 270 – 7440 (max)	Highest levels with propane-fuelled ice resurfacing machines and insufficient ventilation
Ice resurfacing machine: propane petrol electric	69 Indoor ice arenas	2–1838 396 (AM) 283 (AM) 25 (AM)	

[a] AM = arithmetic mean, SD = standard deviation, GM = geometric mean, max = maximum value.

Reference	Project / programme	Country	Averaging time / survey year(s) / methods	Location of measurement
Piechocki-Minguy et al. *(267)*		France	2–24-hour sampling periods (1 during a working day, 1 during the weekend) (personal measurements, diffusion samplers)	4 categories of microenvironment
Pilotto et al. *(27)*		Australia	Hourly peak level (personal exposure)	
Pilotto et al. *(268)*		Australia	9 days (classrooms) 3 days (each household)	Classrooms Dwellings
Ponzio et al. (269)	ECRHS II	Italy (Pavia)	2001–2002	
Raw et al. *(270)*	National representative survey	England	2 weeks in 1997–1999 (Palmes tubes)	Kitchen Bedroom
Riedeker et al. *(271)*		United States (California)	25 work shifts (3 p.m. to midnight) in autumn 2001	
Ross *(272)*		United Kingdom	7-day average and maximum 1-hour average (Palmes samplers)	12 homes
Sabin et al. *(273)*		United States (Los Angeles, CA)	24 morning and afternoon commutes & 10 additional runs	
Saintot et al. *(274)*	THADE SUVIMAX	France	2 periods of 5 consecutive days (1 in winter, 1 in autumn of 1998)	
Sakai et al. *(275)*	INDEX	Sweden (Uppsala) Japan (Nagoya)	24 hours in February through May 1998, 24 hours in February 1998 (diffusion sampler)	Urban dwellings Urban dwellings
Salonen et al. *(43)*			Personal exposure	

Emission source	Number of homes / volunteers	NO_2 measurement results ($\mu g/m^3$) [a]	Comments
		From 17 on summer weekend to 38 on winter weekday	Indoor environments contributed more than 78% to total personal exposure
Unflued gas appliances at home	41 classrooms (388 children)	153 (max)	
Unflued gas heating	10 control schools (unflued gas heating) 8 intervention schools (replacement flued gas or electric heaters installed)	89.91/51.26 (SD, control schools) 29.65/12.62 (SD, intervention schools)	
	114	47.1/24.5 (SD)	
	845 homes	21.8 (GM) 11.9 (GM)	
	Patrol cars	41.7 (mean)	
Kitchen, living room, bedroom		191–1148 (hourly mean)	
	Conventional diesel school buses	64–220; 370 (max)	
	294	43/26.1 (SD) in winter 43.8/20.6 (SD) in autumn	
	27 37	6.7 (GM); 11 (max) 98 (GM); 369 (max)	
Ice resurfacing machines	793 young ice hockey players	21–1176	

[a] AM = arithmetic mean, SD = standard deviation, GM = geometric mean, max = maximum value.

Reference	Project / programme	Country	Averaging time / survey year(s) / methods	Location of measurement
Shima et al. *(10)*	THADE	Japan (Chiba)	24-hour mean (2 × 24 hours, 1 in January or February 1993, 1 in June or July 1993 (passive samplers)	
Simoni et al. *(12)*	INDEX	Italy (Po Delta)	2 weeks (1 in winter, 1 in summer)	
Simoni et al. *(188)*	THADE	Italy (Pisa, urban) Italy (Po Delta, rural)	1 week (summer or winter) in 1991–1994	
Son et al. *(276)*	THADE	Korea (Asan & Chuna)	Passive samplers; house measurements & personal exposure	
Thunqvist et al. *(236)*		Sweden	3 consecutive days (passive diffusion samplers)	
Yang et al. *(46)*		Australia (Brisbane) Republic of Korea (Seoul)	30 consecutive days 21 consecutive days (passive filter badges)	
Zhao et al. *(277)*		China (Taiyuan)		
Zipprich et al. *(278)*		United States (Richmond, VA)	48 hours (personal exposure & indoor concentrations, July to September, passive samplers)	
Zmirou et al. *(279)*		France (Paris, Nice, Toulouse, Clermont-Ferrand, Grenoble)	48 hours (personal exposure & indoor measurements) between 1998 and 2000	Personal exposure & indoor measurements
Zota et al. *(32)*		United States (Boston, MA)	Palmes tubes	Kitchen Living room

Emission source	Number of homes / volunteers	NO_2 measurement results ($\mu g/m^3$) [a]	Comments
	842 schoolchildren	Homes with vented heaters 35.2 (mean) in winter; homes with unvented heaters 32 (mean) in winter	Concentrations in winter very much higher in homes with unvented heaters than in those with vented heaters
	383 adults (homes)	38.26 (median in winter); 26.78 (median in summer); 63.13 (kitchen in winter); 38.26 (kitchen in summer)	
	282 139	28.7 (mean) 42.09 (mean)	
	31 taxi drivers (houses)	47.25 /20.47 (SD in houses); 57.96 /18.56 (SD personal exposure)	Personal exposure more strongly correlated with interior of vehicle
Combustion engine-powered resurfacing machine	9 propane machines 6 electric machines	276 (28–015) 11 (2–30)	
	28 houses 37 houses	15.8 / 18.2 (SD) 44.7 / 38.1 (SD)	I/O ratio 0.88 +/– 0.32
	10 schools	39.4 (mean)	Outdoor levels were 2–3 times higher
	39 adults 9 children in 23 households	30.6 (personal exposure) 24.87 (personal exposure) 34.43 (bedrooms) 36.34 (living rooms)	
	217 pairs of matched 4–14-year-old cases & controls	36.1/21.4 (SD, indoor concentrations); 31.4/13.9 (SD, personal exposure)	Indoor levels higher in the heating season
Gas stove use Reduced air exchange rate during the heating season	77 homes	82.26/38.26 (SD) 68.87/32.52 (SD)	

[a] AM = arithmetic mean, SD = standard deviation, GM = geometric mean, max = maximum value.

Table 5.2. Studies that have examined associations between respiratory symptoms and indoor measurements of or personal exposure to nitrogen dioxide

Reference	Participants	NO_2 exposures in the study
Florey et al. *(148)*	Children	One week mean bedroom (mean): electric cooker 5.64–69.6 µg/m^3; gas cooker 7.52–317.7 µg/m^3
Hoek et al. *(151)*	Children aged 6 years	One-week average (range): kitchen 110–789 µg/m^3; living room 17–277 µg/m^3; bedroom 10–146 µg/m^3
Dijkstra et al. *(150)*	Children aged 6–12 years	Given in Fig. 2 of paper
Koo et al. *(155)*	Children aged 7–13 years	24-hour personal mean: children: 35.9 µg/m^3; mothers: 36.5 µg/m^3
Neas et al. *(153)* (supported by Li et al. *(154)*)	Children aged 7–11 years	Household annual average: without an NO_2 source 16.1 µg/m^3; with an NO_2 source 44.2 µg/m^3
Infante-Rivard et al. *(156)*	Children aged 3–4 years	24-hour personal average: without an NO_2 source 17.3 µg/m^3; with an NO_2 source 32.3 µg/m^3
Samet et al. *(140)*	Infants	Two-week average bedroom: 22% of measures greater than 37.6 µg/m^3
Pilotto et al. *(27)*	Children aged 6–11 years	Winter six-hour average in classrooms: electrically heated, range 13.2–43.2 µg/m^3; gas heated, range 33.8–248.2 µg/m^3
Garret et al. *(152)*	Children aged 7–14 years	Bedroom, living room and kitchen: "indoor" median 11.6 µg/m^3 (5.01–27.9 as 10th & 90th centiles)

Results
Prevalence of respiratory illness: 0–37.6 μg/m^3, 44%; 37.6–75.2 μg/m^3, 59%; > 75.2 μg/m^3, 71%; *P* for trend < 0.05
No association of levels in any of the three locations with symptoms
Odds ratio of symptoms comparing > 60 μg/m^3 Cough 0.80 (0.21–3.05) Wheeze 0.94 (0.37–2.40) Asthma 0.56 (0.15–2.06) No association with lung growth
Unadjusted comparison of mean levels in those with and without symptoms: cough *P* = 0.99 children; asthma *P* = 0.42 children; allergic rhinitis *P* = 0.75 children
Cumulative incidence of respiratory illness: adjusted OR 1.4 (1.14–1.72) per 28.2 μg/m^3
Adjusted OR for asthma: not detectable, 1.00; <18.8 μg/m^3, 0.95 (0.31–2.95); 18.8–28.2 μg/m^3, 3.85 (0.92–16.09); ≥ 28.2 μg/m^3 19.87(4.75–83.03)
No association
Adjusted difference in mean symptom rates for high (≥ 75.2 μg/m^3) compared to low (<75.2 μg/m^3): Sore throat *P* = 0.03 Cough with phlegm *P* = 0.06 Dry cough *P* = 0.9 Wheeze *P* = 0.2 Absent from school *P* = 0.01 Adjusted OR for having at least one day with symptom for high (≥ 75.2 μg/m^3) compared to low (< 75.2 μg/m^3): Sore throat 1.39 (0.80–2.41) Cough with phlegm 1.28 (0.76–2.5) Dry cough 1.08 (0.62–1.90) Wheeze 1.41 (0.63–3.15) Absent from school 1.92 (1.13–3.25)
Adjusted OR per 10 μg/m^3: Cough 1.47 (0.99–2.18) Wheeze 1.15 (0.85–1.54) Asthma attacks 1.06 (0.77–1.46)

Reference	Participants	NO_2 exposures in the study
Magnus et al. *(142)*	Infants from birth to 2 years	Mean living room level 14.7 μg/m^3 (2–43 μg/m^3)
Mukala et al. *(158)*	Pre-school children	Study median 21.1 μg/m^3
Shima et al. *(10)*	Children aged 9–10 years	Mean annual living room: Vented appliances 34.5 μg/m^3 Unvented appliances 60.9 μg/m^3 Winter mean: Vented appliances 45.1 μg/m^3 Unvented appliances 141.1 μg/m^3
Ponsonby et al. *(208)*	Primary school children	Mean personal exposure 19.0 μg/m^3
Emenius et al. *(143)*	Children from birth to 2 years	Mean living room: Urban, no gas stove 16.4 μg/m^3 Urban, gas stove 22.6 μg/m^3 Semi-urban 12.2 μg/m^3 Suburban 8.1 μg/m^3
Belanger et al. *(147)*	Infants who had a sibling with asthma	Two-week mean living area: interquartile range 9.6–32.7 μg/m^3
van Strien et al. *(40)*	Infants from birth to 1 year who had a sibling with asthma	Two-week mean living area: interquartile range 9.6–32.7 μg/m^3
Sunyer et al. *(145)*	Infants	Median in each of three centres: 10.7, 22.2 & 86.2 μg/m^3
Diette et al. *(163)*	Children aged 2–6 years	
Raaschou-Nielsen et al. *(144)*	Infants from birth to 18 months	Mean ten-week average bedroom 8.6 μg/m^3 (95% range 3.3–17.6 μg/m^3)

Results
No association with symptoms of bronchial obstruction and physical signs as identified by physician
Adjusted risk ratio of reporting cough during the same week as measurement: < 16.2 μg/m^3, 1.00; 16.2–27.2 μg/m^3, 1.23 (0.89–1.70); ≥ 27.2 μg/m^3, 1.52 (1.00–2.31) *Adjusted for allergy, stove type, smoking, parental education, day care centre, season*
Adjusted OR per 18.8 μg/m^3 increase: *Boys* Wheeze 0.98 (0.68–1.39) Asthma 0.77 (0.48–1.20) *Girls* Wheeze 1.90 (1.30–2.83) Asthma 1.63 (1.06–2.54)
No association with incidence of wheeze or asthma over 3-year period Difference in post-cold-air challenge FEV_1/FVC ratio per 1.88 μg/m^3: –0.12 (–023 to –0.01) *Adjusted for height, sex, technician, smoking exposure, days between NO_2 measurements, spirometry*
Recurrent wheezing: < 8.4 μg/m^3, 1.00; 8.4–11.7 μg/m^3, 0.97 (0.42–2.24); 11.7–15.6 μg/m^3, 1.17 (0.46–2.99); > 15.6 μg/m^3, 1.48 (0.91–2.42) *Adjusted for gender, family history of asthma, smoking, breastfeeding, age of building*
Persistent cough per 18.8 μg/m^3 increase in living room NO_2: 1.21 (1.05–1.40) *NB: most of the pertinent data from this study presented in paper by van Strien (40)*
Adjusted relative rate of symptoms (1st, 2nd, 3rd, 4th quartiles of NO_2): Wheeze 1.00; 1.15 (0.79–1.67); 1.03 (0.69–1.53); 1.45 (0.92–2.27) Persistent cough 1.00; 0.96 (0.69–1.36); 1.33 (0.94–1.88); 1.52 (1.00–2.31) Shortness of breath 1.00; 1.59 (0.96–2.62); 1.95 (1.17–3.27); 2.38 (1.31–4.34) *Quartile cut-offs for analyses 5.1, 9.9, 17.4 μg/m^3* *Adjusted for season, parental asthma, mother's ethnicity, mother's education, smoking in the home, day care, living in an apartment, presence of siblings, gender, nitrous acid*
Adjusted OR for lower respiratory tract illness: < 9.4 μg/m^3, 1.00; 9.4–18.8 μg/m^3, 0.88 (0.63–1.23); 18.8–56.4 μg/m^3, 0.99 (0.69–1.43); ≥ 56.4 μg/m^3, 1.31 (0.75–2.26)
Median (IQR) three-day bedroom NO_2 (μg/m^3): children without asthma, 39.3 (26.3–58.3); children with asthma, 40.6 (26.3–63.9); $P = 0.84$
Adjusted odds of wheezing in first 18 months: < 5.2 μg/m^3, 1.00; 5.2–6.8 μg/m^3, 0.66 (0.27–1.61); 6.8–8.6 μg/m^3, 0.80 (0.32–2.01); 8.6–11.7 μg/m^3, 1.15 (0.40–3.32); ≥ 17.7 μg/m^3, 0.43 (0.15–1.18) *Adjusted for sex, area, mother's education, lung function*

Reference	Participants	NO_2 exposures in the study
Morales et al. *(146)*	Children aged 4 years	Median two-week average living room 21.6 µg/m^3; range 0.8–185.9 µg/m^3
Adults		
Keller et al. *(180,181)*	Adults	Mean 24-hour average. cooking with electricity 37.6 µg/m^3 ; cooking with gas 94.0 µg/m^3
Fischer et al. *(185)*	Women aged 40–60 years	Weekly mean: kitchen 18.8 –735 µg/m^3 ; living room 15.1–372.4 µg/m^3 ; bedroom 15.1–99.6 µg/m^3
Koo et al. *(155)*	Mothers	Personal NO_2: user of LPG/kerosene (no fan) 37.7 µg/m^3; user of LPG/ kerosene (fan) 41.7 µg/m^3
Simoni et al. *(188)*	Population-based sample	Seven-day mean indoor (average of kitchen, bedroom and living room): Pisa summer 24.4 µg/m^3; Po Delta summer 28.2 µg/m^3; Pisa winter 28.2 µg/m^3; Po Delta winter 41.4 µg/m^3
Triche et al. *(186)*	Mothers	Two-week average No source: median 25.3 µg/m^3; max 276 µg/m^3; source: median 22.7 µg/m^3; max 312.8 µg/m^3
Studies in asthmatics		
Smith et al. *(160)*	Asthmatics (children and adults)	Personal indoor daily mean 6.9–275.6 µg/m^3
Chauhan et al. *(165)*	Asthmatics	Geometric mean personal exposure 10.6 µg/m^3
Pilotto et al. *(268)*	Children with asthma (randomized controlled trial)	Six-hourly average levels: intervention classes 13.2–71.4 µg/m^3; non-intervention classes 22.5–218.1 µg/m^3

Results
Change in cognitive function score (95% CI) per 1.88-μg/m^3 increase; GSTP genotype: Ile/Ile 0.10 (– 0.22 to 0.42); Ile/Val or Val/Val –0.55 (– 0.86 to –0.25); *P* for interaction = 0.04
Adjusted OR (95% CI) of inattention symptoms; GSTP genotype: Ile/Ile 0.98 (0.88–1.09); Ile/Val or Val/Val 1.11 (1.03–1.20); *P* for interaction = 0.26 *Adjusted for maternal social class, maternal education, school age, observer, maternal smoking in pregnancy, number of smokers in home, maternal alcohol consumption during pregnancy, home location*
No association with respiratory illness observed
Adjusted difference in annual decline in FEV_1 (se) per unit change in NO_2: kitchen –0.025 ml (0.021); living room –0.048 ml (0.043); bedroom –0.164 ml (0.165)
Personal exposure level Without chronic cough 35.9 μg/m^3; with chronic cough 42.3 μg/m^3; *P* = 0.05 Without allergic rhinitis 35.5 μg/m^3 ; with allergic rhinitis 42.4 μg/m^3; *P* = 0.002
Generated personal exposure as product of hours per day indoors and measured indoor levels Divided exposure into two categories (above and below the median) Adjusted OR for acute respiratory symptoms with fever (high vs low): 1.66, 95% CI 1.08–2.57 No association with asthma/bronchitic symptoms without fever, or with peak flow, or with irritant symptoms, or with non-specific symptoms (values not given) *Adjusted for sex, age, active smoking and area of residence*
Adjusted OR of symptom comparing > 150.4 μg/m^3 with other measures: wheeze 4.00 (1.45–11.0); chest tightness 1.94 (0.98–3.85)
Adjusted OR in under 14-year-olds: wheeze 1.04 (0.89–1.12); cough 1.07 (0.89–1.29); daytime attacks of asthma 1.13 (1.02–1.26) No associations seen in other age groups
Risk of asthma exacerbation following infection
Mean rate ratio (intervention vs control) Difficulty breathing in day 0.41 (0.07 –0.98) Difficulty breathing at night 0.32 (0.14–0.69) Chest tightness 0.45 (0.25–0.81) Asthma attacks during the day 0.39 (0.17–0.93)

Reference	Participants	NO_2 exposures in the study
Nitschke et al. *(168)*	Children with asthma aged 5–13 years	Indoor daily mean (range): classrooms 16.9–577.2 µg/m^3; kitchens 5.6–795.4 µg/m^3
Belanger et al. *(164)*	Children with asthma aged < 12 years	Median average 10-day living room: homes without a source 16.2 µg/m^3; homes with a source 48.7 µg/m^3 Mean average 10-day living room: single-family homes 19.2 µg/m^3; multi-family housing 43.1 µg/m^3
Delfino et al. *(161)*	Children with asthma aged 9–18 years	Personal exposure: range 5.1–198.7 µg/m^3
Delfino et al. *(162)*	Children with asthma aged 9–18 years	Personal exposure: range 5.1–198.7 µg/m^3
Kattan et al. *(23)*	Children with asthma aged 4–9 years	Bedroom: median 56.0 µg/m^3 (0.9–902.4 µg/m^3)
Hansel et al. *(26)*	Children with asthma aged 2–6 years (same asthmatic children as included in Diette et al. *(163)*)	Mean three-day average bedroom: without gas stove 31.6 µg/m^3; with gas stove 62.3 µg/m^3
Ng et al. *(191)*	Adults with asthma	NO_2 levels measure while cooking: highest peak seen 500 µg/m^3; personal exposure 37.6–135.6 µg/m^3

Results
Adjusted relative rates of symptoms per 18.8 μg/m^3 increase NO_2 Classroom: Nocturnal wheeze 0.99 (0.93–1.06) Nocturnal cough 1.01 (0.98–1.04) Nocturnal asthma attacks 1.00 (0.93–1.08) Nocturnal difficulty breathing 1.11 (1.05–1.18) Kitchen: Nocturnal wheeze 1.00 (0.90–1.11) Nocturnal cough 0.99 (0.96–1.02) Nocturnal asthma attacks 1.04 (1.00–1.07) Nocturnal difficulty breathing 1.03 (1.01–1.05) Mean FEV_1 predicted –0.39% per 18-μg/m^3 increase in NO_2 No consistent evidence of interaction of NO_2 with Der p 1
Adjusted OR of any symptom per 37.6 μg/m^3 increase Single-family home: wheeze 0.99 (0.71–1.38); cough 1.07 (0.84–1.35); chest tightness 1.10 (0.78–1.57) Multi-family housing: wheeze 1.52 (1.04–2.21); cough 1.06 (0.75–1.49); chest tightness 1.61 (1.04–2.49)
Increase in FeNO: 1.6 ppb per 32-μg/m^3 increase in personal NO_2
Change in FEV_1 as percentage of predicted FEV_1: –2.45 (–1.33 to –3.57)
Highest quartile compared to lowest three quartiles: More than 4 days of symptoms in last fortnight 1.75 (1.10–2.78) in non-atopics; 1.12 (0.86–1.45) in atopics
Adjusted incidence ratio for symptoms per 37.6 μg/m^3 increase: limited speech due to wheeze 1.17 (1.08–1.27); coughing without a cold 1.15 (1.07–1.23); nocturnal symptoms 1.12 (1.04–1.19)
Fall in peak flow was related to level of NO_2 measured while cooking

6. Polycyclic aromatic hydrocarbons

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General description

The term polycyclic organic matter (POM) defines a broad class of compounds that generally includes all organic structures containing three or more fused aromatic rings. These structures can contain the elements carbon, hydrogen, oxygen, nitrogen and sulfur.

POM containing up to seven fused rings has been identified, and theoretically millions of POM compounds could be formed; however, only about 100 species have been identified and studied. The most common subclass of POM is the polycyclic aromatic hydrocarbons (PAHs). These compounds contain only carbon and hydrogen *(1)*.

PAHs are a large group of organic compounds with two or more fused aromatic (benzene) rings *(2)*. Low-molecular-weight PAHs (two and three rings) occur in the atmosphere predominantly in the vapour phase, whereas multi-ringed PAHs (five rings or more) are largely bound to particles. Intermediate-molecular-weight PAHs (four rings) are partitioned between the vapour and particulate phases, depending on the atmospheric temperature *(3)*. Particle-bound PAHs are considered to be very hazardous to human health. Benzo[*a*]pyrene (B[*a*]P) is often used as a marker for total exposure to carcinogenic PAHs, as the contribution of B[*a*]P to the total carcinogenic potential is high (in one study reported as being in the range 51–64%) *(4)*.

B[*a*]P (CAS Registry Number, 50-32-8; $C_{20}H_{12;}$ molecular weight = 252.31 g/mol) is a pale yellow monoclinic crystal with a faint aromatic odour. It has a melting point of 179 °C, a high boiling point of 496 °C at 1 atm, a Henry's Law constant of 4.8×10^{-5} kPa.m^3/mol and a low vapour pressure of 7.3×10^{-7} Pa at 25 °C. As a consequence of these physical properties, B[*a*]P is predominantly particle phase rather than gas phase.

PAHs have a relatively low solubility in water (e.g. solubility in water of B[*a*]P at 25 °C is 3.8 µg/l) but are highly lipophilic (e.g. B[*a*]P log K_{ow} = 6.04)[1] and are soluble in most organic solvents. Once adsorbed on to soil, PAHs have low mo-

[1] The octanol–water partition coefficient (K_{ow}) is a measure of the hydrophobicity of a compound. It is a measure of the distribution of a compound between water and an organic (octanol) with which is in contact *(6)*.

bility (e.g. B[*a*]P log K_{oc} = 6.6–6.8).[2] Therefore, once released into the environment and owing to their low aqueous solubility, elevated octanol–water and organic carbon coefficients as well and high melting and boiling points, PAHs have a tendency to be associated with particulate matter, soils and sediments *(2,5)*.

In the atmosphere, PAHs may be subject to direct photolysis, although adsorption to particulates can retard this process. PAHs can also react with pollutants such as ozone, hydroxyl radicals, nitrogen dioxide and sulfur dioxide, yielding diones, nitro- and dinitro-PAHs, and sulfonic acids, respectively *(2)*. PAHs may also be degraded by some fungi and microorganisms in the soil and can be metabolized by a wide variety of terrestrial and aquatic organisms *(7)*, although they are expected to bioconcentrate in organisms (aquatic and terrestrial) that cannot metabolize them *(2,8)*.

Conversion factors

At 760 mmHg and 20 °C, 1 ppm of B[*a*]P = 10.494 mg/m^3 and 1 mg/m^3 = 0.095 ppm; at 25 °C, 1 ppm of B[*a*]P = 10.318 mg/m^3 and 1 mg/m^3 = 0.097 ppm *(9)*.

Sources and pathways of exposure

Sources

PAHs are widespread environmental pollutants that are formed in the combustion process of carbonaceous materials at high temperature *(10)*. Indoor air is contaminated by PAHs, which come not only from infiltration or intrusion of outdoor air but also from indoor emission sources such as smoking, cooking, domestic heating with fuel stoves and open fireplaces, as well as from incense and candle emissions *(11–16)*.

For lower-molecular-weight PAHs, the impact of house characteristics and indoor activities tends to be greater than the influence of the penetrating outdoor air. On the other hand, while indoor sources may exist for PAHs with two or three rings, outdoor air may contribute significantly to the indoor PAHs, especially those with four or more rings *(17)*.

Emissions from traffic have been found to be the main outdoor source for the indoor PAH concentration at urban and suburban locations in many industrialized countries *(18)*. Motor vehicle emissions account for around 46–90% of the mass of individual PAHs in ambient air particles in urban areas *(19)*, while domestic heating can account for some 16% of PAHs in outdoor air in the United States, 29% in Sweden and 33% in Poland, as reported in the early 1980s *(20)*. Other outdoor sources of PAHs are industrial plants, power generation plants, waste incinerators and open burning. The age of a house or building, since it reflects its condition, affects PAH concentrations indoors. For example, the older

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[2] The organic carbon coefficient (K_{oc}) is a measure of a chemical compound's mobility in soil and the prevalence of leaching from soil *(6)*.

a house the higher the PAH concentrations will be, as outdoor sources have a greater impact owing to higher air exchange through such routes as poorly fitting windows *(21)*.

In industrialized countries, ETS appears to have the greatest impact on the total PAH concentration indoors and it is identified as the single largest source of PAHs in the indoor environment, with significant emission factors associated with smoking *(22)*. Although reductions in the emission of PAHs in mainstream cigarette smoke have been reported (Table 6.1), the concentration of B[*a*]P in a room extremely polluted with cigarette smoke could still be as high as 22 ng/m^3 *(23)*. In smokers' homes, more than 87% of the total PAHs may be attributable to this source. On the other hand, background sources are the largest contributor to PAHs in non-smokers' homes *(24)*.

Cooking and heating with solid fuels such as dung, wood, agricultural residues or coal, especially in unvented or flueless stoves, is likely to be the largest source of indoor air pollution globally owing to the high level of use of these fuels in developing countries. More than 75% of people in China, India and nearby countries, and 50–75% of people in parts of Africa and South America, use solid fuel for cooking *(25)*.

Concerning data reported on emission factors for B[*a*]P (Table 6.1) and PAHs (Table 6.2) from different fuels, these can be ranked as briquettes < wood < wood/root-fuel mixtures according to their polluting potential, and natural gas < coal < briquettes < wood according to their B[*a*]P and PAH emission factors, respec-

Table 6.1. Benzo[*a*]pyrene emission factors

Source	Emission factor	Unit	Comment	Reference
Cigarettes	35	ng/cigarette	Average content in mainstream smoke before 1960	WHO *(23)*
	18	ng/cigarette	Average content in mainstream smoke, 1978–1979	WHO *(23)*
Fuel	0.8 1.6–8.2 5.3–13.2	mg/kg mg/kg mg/kg	Peat briquettes Wood Mixture of wood and root-fuel	Kakareka et al. *(26)* Kakareka et al. *(26)* Gupta et al. *(27)*; Venkataraman et al. *(28)*
Candles	n.d.–0.13[a]	ng/g of wax burned	Candles	Lau et al. *(16)*
Creosote	58–749	µg/g	Creosote-impregnated wood products	Ikarashi et al. *(29)*

[a] n.d. = not determined.

Table 6.2. PAH emission factors

Source	Emission factor	Units	Comment	Reference
Fuel	1–2000	pg/kg	Natural gas	Rogge et al. *(30)*
	0.95–2.0	mg/kg	Coal	Oanh et al. *(31)*
	2.8–3.0	mg/kg	Briquettes	Venkataraman et al. *(28)*
	2.0–114	mg/kg	Wood	Venkataraman et al. *(28)*; Oanh et al. *(31)*; Schauer et al. *(32)*; Ravindra et al. *(33)*
Candles	4.75–156	ng/g of wax burned	Candles	Lau et al. *(16)*

Note: Different authors might report different groups of PAHs.

tively. However, caution should be exercised, as different studies report different ranges of compounds, which might not be comparable. Data on emission factors from burning candles show that this source emits less than cigarettes and fuels *(16)*.

Wood burning in fireplaces and wood/solid fuel stoves is used as the main source of heating in developing countries and as a secondary heating source in countries with a cold winter climate. The burning of fossil fuel, solid fuel and biomass has been recognized as an important source of airborne PAHs as it releases a wide range of air pollutants, including PAHs, which are emitted to the indoor atmosphere in unvented or flueless combustion and also to the outdoor air *(34)*. Even in airtight stoves with a flue, elevated indoor levels of PAHs can result from intrusion of outdoor air and/or leakage from wood-burning appliances *(35)*.

High concentrations of particulate PAH compounds have been reported in indoor environments during the burning of fossil fuels and biofuel for cooking *(36)*, generally in unvented stoves, suggesting that exposure during the cooking period is 2–10 times higher than ambient exposure *(37)*. Concentrations of PAHs and B[*a*]P indoors, using different types of cooking fuel, increased in the order LPG < kerosene < coal < wood < dung cake/wood mixture < dung cake as reported in Tables 6.3 and 6.4, respectively. Transient high concentration peaks were reported in measurements performed during cooking *(38)*.

Apart from cooking fuel being a source of PAHs, generated particularly in unvented stoves, cooking practice (e.g. charring meat, deep frying) is another source of PAHs generated during cooking. The emissions from cooking practice depend greatly on the cooking method used, the fat content of the food and the quantity of food being cooked. Food with a higher fat content emits more PAHs than low-fat food *(41)*. Also, an increase in cooking temperature generally increases the production of most PAHs *(3)* because there is an increase firstly in the evaporation of PAHs from heated oils into the air and secondly there is an increase in the PAHs generated by pyrolysis from partially cracked organic compounds in food and cooking oils *(3,42)*. A comparative study of cooking

Table 6.3. Indoor PAH concentrations associated with different sources

Source	Concentration (μg/ m^3)	Comment	Reference
ETS	0.02–0.84	Pubs and restaurants (16 PAHs) [a]	Harrison et al. *(39)*; Bolte et al. *(40)*
Fuel	0.11	LPG for cooking	Raiyani et al. *(36)*
	0.27–0.31	Kerosene for cooking	Raiyani et al. *(36)*
	1.22–1.9	Cattle dung and wood as cooking fuel	Raiyani et al. *(36)*
	2.01	45–60 minutes, 16 PAHs,[a] wood as cooking fuel	Raiyani et al. *(38)*
	3.46	45–60 minutes, 16 PAHs,[a] wood dung cake as cooking fuel	Raiyani et al. *(38)*
	3.56	45–60 minutes, 16 PAHs,[a] dung cake as cooking fuel	Raiyani et al. *(38)*
Cooking	7.6	Chinese domestic cooking, 12 PAHs [b]	Zhu & Wang *(41)*
Heating	0.164	Kerosene stoves in Indian homes, 12 PAHs [b]	Pandit et al. *(37)*

[a] The 16 PAHs comprised naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, benzo[*a*]pyrene, indeno[1,2,3-*cd*]pyrene, dibenz[*a,h*]) anthracene and benzo[*ghi*]perylene.

[b] The 12 PAHs comprised naphthalene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benz[*a*]anthracene, chrysene, benzo[*k*]fluoranthene, benzo[*e*]pyrene and benzo[*a*]pyrene.

Note: Different authors might report different groups of PAHs.

practices showed that boiling produced the least PAHs, while broiling and frying produced most PAHs *(43)*.

Varying amounts of PAHs are present in creosote, which has been traditionally used as a wood preservative in the foundations of buildings, in fences and in the manufacture of garden furniture and outdoor recreational facilities in parks. B[*a*]P levels of 58–749 μg/g were found in creosote-impregnated wood products *(29)*.

The EU restricts creosote applications inside buildings *(44)* and Japan restricts the B[*a*]P content in creosote *(45)*, but creosote-treated wood might be an indoor source in other parts of the world.

Finally, mothball storage is associated with significant levels of naphthalene *(39,46)*, acenaphthalene, phenanthrene and fluorene indoors *(46)*.

Routes of exposure

Humans are exposed to PAH through several routes, namely inhalation of air and re-suspended soil and dust, consumption of food and water, and dermal contact with soil and dust *(65)*. All these sources are relevant to global human exposure. However, while soil contact generally occurs outdoors and food and water consumption is usually indoors, inhalation leads to exposure both indoors and outdoors. Yet people spent 80–93% of their time indoors, and hence indoor air would be the most relevant source contributing to the inhalation route *(66)*.

Table 6.4. Indoor benzo[*a*]pyrene concentrations associated with different sources

Source	Concentration (ng/m^3)	Comment	Reference
ETS	22	Extremely ETS polluted	WHO *(23)*
	0.23–1.7	Homes with ETS in industrialized countries	Chuang et al. *(22)*; Mitra & Ray *(24)*; Harrison et al. *(39)*; Fromme et al. *(47)*
	0.01–0.58	Homes without ETS in industrialized countries	Chuang et al. *(22)*; Mitra & Ray *(24)*; Harrison et al. *(39)*; Fromme et al. *(47)*
	1.45–4.1	Pubs and discotheques	Harrison et al. *(39)*; Bolte et al. *(40)*
Fuel	0.2–17.6	Kerosene as cooking fuel, geometric mean	Aggarwal et al. *(48)*
	33	Coal as cooking fuel, geometric mean	Aggarwal et al. *(48)*
	120–186	Cattle dung and wood as cooking fuel, geometric mean	Aggarwal et al. *(48)*
	1300–9300	Cattle dung and wood as cooking fuel, peak values over 15–30 minutes	Aggarwal et al. *(48)*
Cooking	6–24	Chinese domestic cooking, 12-PAH	Zhu & Wang *(41)*
Heating	2–490	Use of non-airtight stoves	Traynor et al. *(49)*
	0.63	Use of airtight stoves burning wood	Traynor et al. *(49)*; Daisey et al. *(50)*
	70	Unvented fireplaces in Burundi homes	Viau et al. *(51)*
	6.9	Kerosene stoves in Indian homes	Pandit et al. *(37)*
	33–166	Heating using coal, wood and cattle dung	Aggarwal et al. *(48)*
Unspecified source	0.05–0.44	American homes	Chuang et al. *(22)*; Mitra & Ray *(24)*; Van Winkle & Scheff *(46)*; Turpin et al. *(52)*; Naumova et al. *(53)*; Chuang et al. *(54)*
	0.01–0.65	European homes	Gustafson et al. *(34)*; Harrison et al. *(39)*; Fromme et al. *(47)*; Kingham et al. *(55)*; Fischer et al. *(56)*; Minoia et al. *(57)*
	1.42	Italian homes, max	Menichini et al. *(58)*
	0.09–25.52	Polish homes	Choi et al. *(59)*
	0.21–3.4	Asian urban homes	Li & Ro *(14)*; Sugiyama et al. *(60)*; Chao et al. *(61)*; Saito et al. *(62)*; Ohura et al. *(63)*; Azuma et al. *(64)*
	0.3 (0.01–1.25)	United Kingdom offices	Harrison et al. *(39)*
	0.03–0.07	Libraries and museums	Harrison et al. *(39)*

Air

The potential doses of carcinogenic PAHs[3] were estimated using the standard EPA recommendation for an individual's respiration rate *(67)* and applying this factor to the range of concentrations reported in the section of this chapter dealing with indoor levels and their relation to outdoor levels (page 301). The recommended value for the average inhalation rate of the general population is 11.3 m^3/day for women and 15.2 m^3/day for men *(67)*. Considering the different B[*a*]P indoor air concentrations reported, and using the adult male inhalation rate as a worst-case scenario, the daily intake dose due to inhalation spans the range of 0.15–32 ng/day. However, higher daily levels of inhaled B[*a*]P can be experienced during exposure to specific indoor sources such as cooking with different fuels (91–2523 ng/day) or using non-airtight stoves for heating (30–7448 ng/day) *(36)* (Table 6.5).

Table 6.5. Benzo[*a*]pyrene inhalation daily dose

Source	Daily dose (ng/day)	Comment	Reference
General	0.15–21	Homes in industrialized countries	See methodology described in the text
	3–26	Asian homes	
	6–21	Public indoor spaces in the United Kingdom and the United States	
Cooking	91–365	Chinese kitchens	
	105	Cooking with kerosene	Raiyani et al. *(38)*
	502	Cooking with wood	Raiyani et al. *(38)*
	2523	Cooking with cattle dung	Raiyani et al. *(38)*
Heating	30–7448	Indoors using non-airtight stoves	Raiyani et al. *(38)*
ETS	4–15	ETS-polluted indoors	See footnote 4
	1.3–6.7	Non-ETS-polluted indoors	
	26–62	Pubs and discotheques	

ETS is an important contributor to the inhalation source of PAHs. Using the same methodology as describe above,[4] daily inhalation of B[*a*]P in indoor environments would range from 4 to 15 ng/day in ETS-polluted compared with 1.3–6.7 ng/day in homes not exposed to ETS. The daily (24-hour) inhalation can be as high as 26–62 ng/day in pubs and discotheques. Children's daily exposures, expressed as urinary cotinine levels (a biomarker of tobacco smoke) were 8.1 µg/l urine in ETS-exposed children compared to 2.7 µg/l in children not exposed to ETS *(68)*.

[3] Carcinogenic PAHs include benz[*a*]anthracene, benzo[*a*]pyrene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, chrysene, dibenzo[*a,h*]anthracene, benzo[*ghi*]perylene and indeno[1,2,3-*cd*]pyrene.

[4] Calculated using the concentrations reported by Mitra & Ray 1995 and Fromme et al. 1995 and applying the USEPA 1997 male individual's breathing rate.

Drinking-water

Several studies performed in the United States reported values of carcinogenic PAHs for drinking-water in the range 0.1–61.6 ng/l, although most of the values fell between 1 and 10 ng/l. In the case of B[*a*]P, all the values were below the limit of detection (0.1 ng/l) *(65,69)*. Similarly, the examination of a number of drinking-water supplies for six PAHs (fluoranthene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, B[*a*]P, benzo[*g,h,i*]perylene and indeno[1,2,3-*c,d*]pyrene) indicated that the collective concentrations generally did not exceed 100 ng/l. The concentrations of these six PAHs were between 1 and 10 ng/l in 90% of the samples and higher than 110 ng/l in 1% *(23,70)*.

As regards the concentrations of the 16 PAHs, these span the range of 106.5–150.3 ng/l in several European and Canadian cities *(71)*, while lower values of 85.2–94.6 ng/l have been reported in Taiwan, China *(72)*. Studies performed in Europe have reported levels of B[*a*]P in the range of < 1 ng/l in Germany *(73)* to 10 ng/l in Poland *(74)*. Values of B[*a*]P in the same range (1.4–2.5 ng/l) have also been reported in Taiwan, China *(72)*.

Assuming an average drinking-water consumption of 2 l/day, the potential dose of carcinogenic PAHs via drinking-water ranged from 0.2 to 123 ng/day, 170–300 ng/day for the 16 PAHs and < 2–20 ng/day for B[*a*]P .

Food

PAHs are found in substantial quantities in some foods, depending on the method of cooking, preservation and storage, and intake is influenced by personal eating habits *(75)*. PAHs are detected in a wide range of meats, fish, vegetables and fruits, fluoranthene and B[*a*]P being the two PAHs detected at highest levels in food with fluoranthene levels exceeding those of B[*a*]P *(76,77)*. Food groups that tend to have the highest levels of PAHs and B[*a*]P include charcoal-broiled or smoked meats, fats and oils, and some leafy vegetables and grains. For these food groups, concentrations of 16 PAHs were typically in the tens of micrograms per kilogram (Table 6.6) *(78–81)*. However, the PAH load on leafy vegetables and grains can be removed by washing. As regards B[*a*]P, recent studies report that food containing fat show the highest levels of B[*a*]P, with maximum levels of 60 μg/kg (Table 6.7) *(65,75,82)*. Lower levels of B[*a*]P in the range of hundreds of nanograms per kilogram have been reported in more recent studies for fruits and vegetables, sweets, dairy products, beverages, bread, cereals, grains and seafood *(83,84)*.

A Dutch "market basket" study of dietary components for 18-year-old males, involving the determination of 17 different PAHs,[5] revealed that all of

[5] The 17 PAHs comprise naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo[*j*]fluoranthene benzo[*k*]fluoranthene, benzo[*a*]pyrene, indeno[1,2,3-*cd*]pyrene, dibenz[*a,h*])anthracene, benzo[*ghi*]perylene.

these compounds were detected. The most frequently occurring were benzo[*b*] fluoranthene, fluoranthene and benzo[*k*]fluoranthene in 59%, 48% and 46% of the samples, respectively. The highest concentration of a single PAH was found for chrysene, at 36 μg/kg in the commodity group "sugar and sweets". The mean daily intake of the total PAH fraction (17 PAHs) analysed ranged between 5 and 17 μg/day. The intake of the carcinogenic PAH fraction was roughly half of these

Table 6.6. The 16-PAH content of foods

Location	Concentration (μg/ kg)	Comment	Reference
General	8–71	Fish and seafood	Bordajandi et al. *(80)*; Douabul et al. *(81)*
	13.4–25.56	Meat products	Marti-Cid et al. *(78)*; Falco et al. *(79)*
	23.48	Oils and fats	Marti-Cid et al. *(78)*; Falco et al. *(79)*
	14.5–44	Cereals	Marti-Cid et al. *(78)*; Falco et al. *(79)*

Table 6.7. Benzo[*a*]pyrene content of foods

Location	Concentration (μg/ kg)[a]	Comment	Reference
General	0.001–0.22	Potatoes	Jakszyn et al. *(82))*
	0.003–0.48	Vegetables	
	n.d.–3.37	Fruit	
	n.d.–1.60	Milk and dairy products	
	n.d.–5.4	Cereals	
	n.d.–4.60	Meat	
	n.d.–11.2	Fish and seafood	
	n.d.–58.2	Fats	
	0.01–0.44	Sweets and desserts	
	0.009–0.36	Beverages	
United States, 1990	0.1–15	Smoked food	Lioy & Greenberg *(75)*
	3–29.3	Charcoal-broiled food	
	0.1–48.1	Vegetables, fruit and cereals	
United States, 2001	0.01–4.86	Beef and chicken	Kazerouni et al. *(83*
	0.01–0.13	Pork	
	0.01–0.24	Seafood	
	0.01–1.75	Restaurant/fast-food meat	
	0.01–0.18	Dairy products, fat products and beverages	
	0.02–0.56	Bread, salty snacks, cereals and grains	
	0.01–0.47	Sweets and desserts	
	0.01–0.48	Fruit and vegetables	
Republic of Korea, 2007	5.4	Fried chicken or dried beef	Lee & Shim *(84)*
	0.36	Sesame oil	
	0.44	Peanuts	

[a] n.d. = not determined.

amounts. The largest contribution to the daily PAH intake came from sugar and sweets, cereals, oils, fats and nuts *(85)*.

For the average American diet, the intake of carcinogenic PAHs was estimated to be 1–5 μg/day, with unprocessed grains and cooked meats the greatest sources of the compounds *(65)*. This is lower than in a recent study in Spain, where the dietary intake of carcinogenic PAHs[6] ranged from 723 to 969 ng/day and the 16 PAHs ranged from 8.57 to 13.81 μg/day *(78,86)*.

The dietary intake of B[*a*]P ranged between 0.002 and 1.1 μg/day in the United States in the late 1980s *(69)*. However, lower levels were reported in a recent study, similar to those reported in Asia and Europe, ranging from 4.2 to 320 ng/day (Table 6.8). The lowest daily intake for B[*a*]P and 16 PAHs has been reported in Yemen (1.7 and 167 ng/day, respectively) based on the fish consumption of the Yemeni population *(81)*.

Table 6.8. Benzo[*a*]pyrene daily dietary intake dose

Location	Daily dose (ng/day)	Comment	Reference
United States	0.002–1100	United States, 1988	Lioy et al. *(69)*
	0.5–305	United States, 2005	Anderson et al. *(87)*
Asia	70–190	Islamic Republic of Iran and Republic of Korea	Lee & Shim *(84)*; Hakami et al. *(88)*
	1.7	Yemen	Douabul et al. *(81)*
Europe	160–320	Italy	TurrioBaldassarri et al. *(89)*
	73–140	Spain	Marti-Cid et al. *(78)*; Ibanez et al. *(86)*
	4.2–35.0	Czech Republic	Kulhanek et al. *(90)*

Soil

Carcinogenic PAHs are found in all surface soils *(65)*. Typical concentrations in forest soil range from 5 to 100 μg/kg (Table 6.9). Substantial amounts of PAHs are transferred to forest soil from vegetative litter because the compounds are adsorbed from air onto organic matter such as leaves and pine needles. Rural soil contains carcinogenic PAHs at levels of 10–100 μg/kg, originating mainly from atmospheric fallout. For both forest and rural soil, values as high as 1000 μg/kg may occasionally be found *(65,91,92)*.

Metropolitan areas have higher PAH concentrations than forest and agricultural areas because of the many sources of fossil fuel combustion. The majority of urban soil concentrations fall in the 600–3000-μg/kg range *(65,93,94)*. Higher

[6] Carcinogenic PAHs from this study include benz[*a*]anthracene, benzo[*a*]pyrene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, chrysene, dibenzo[*a,h*]anthracene and indeno[1,2,3-*cd*]pyrene.

Table 6.9. PAH content of soils

Location	Concentration (mg/kg)	Comment	Reference
General	0.01–0.1	Rural soil	Menzie et al. *(65)*
	0.05–0.1	Forest soil	Menzie et al. *(65)*
	1.0	Forest and rural soil peaks	Nam et al. *(91)*
	0.6–3.0	Urban soil	Menzie et al. *(65)*
	1.0–3.0	Heavy transportation and industrialized	Menzie et al. *(65)*; Trapido *(93)*; Mielke et al. *(94)*
Europe	14.6–99.6	United Kingdom, 17 PAHs, roadside soil	Harrison et al. *(95)*
	2.02	United Kingdom, 17 PAHs, urban soil	
United States	8–336	Road dust in cities	Menzie et al. *(65)*
Asia	0.20–1.15	Lahore, Pakistan, 17 PAHs	Smith et al. *(92)*

values near areas of heavy transportation and industrialization range from 8 to 336 mg/kg *(65,95)*. Values in the order of 1000–3000 μg/kg are regarded as being in the upper range.

As regards B[*a*]P levels in topsoil (Table 6.10), the lowest concentrations are found in tropical rural and urban soils (0.3–5.5 μg/kg) and the highest in arable and forest areas in temperate latitudes (18–39 μg/kg) *(96)*. The highest concentrations were found in urban areas, with values ranging from 5.5 to 379 μg/kg *(96–100)* and from 971 to 1600 μg/kg in large United Kingdom cities and Chicago *(97)*. Levels in industrialized areas across the world ranged between 18 and 360 μg/kg *(99,101,102)*.

Incidental ingestion of soil by adult males was estimated to be of the order of a few milligrams per day. Soil ingestion rates of the order of 100 mg/day are more typical for small children *(103)*. Therefore, the potential dose of carcinogenic PAHs for urban populations ranged from 0.2 to 96 ng/day (median 7 ng/day).

Relative importance of different routes of exposure

Human exposure will be from both inhalation of contaminated air and consumption of contaminated food and water. Especially high exposure will occur through the smoking of cigarettes and the ingestion of certain foods (e.g. smoked and charcoal-broiled meats and fish) *(2)*. Food ingestion is likely to be a larger route of exposure compared to inhalation for a large section of the general population exposed to PAHs. Drinking-water and soil are generally minor sources of these compounds in the daily intake dose *(65)*.

In an earlier American study, diet was reported to make a substantial contribution (generally more than 70% in non-smokers) to PAH intake other than occupational PAH exposure. For a non-smoking reference male (70 kg body weight),

Table 6.10. Benzo[*a*]pyrene content of soils

Location	Concentration (μg/ kg)	Comment	Reference
General	18–19	Arable and grassland areas	Wilcke *(96)*
	39	Forest areas	
	350	Urban areas	
	0.3–2.0	Tropical topsoil for rural forest in the Amazon and Ghana	
	5.2–5.5	Urban tropical areas, Brazil and Thailand	
Europe	43–236	Urban areas, Baltic countries	Saltiene et al. *(97)*
	76–229	Urban areas, southern Europe	Morillo et al. *(98)*
	971–1600	Large cities, United Kingdom	Saltiene et al. *(97)*
	7–379	Rural and urban areas, United Kingdom	Wild & Jones *(100)*
	18–100	Spanish industrial areas	Nadal et al. *(99)*
	56–22	Spanish residential areas	Nadal et al. *(99)*
	360	Polish heavy industrialized areas	Bodzek et al. *(74)*
	22	Polish urban areas	Maliszewska-Kordybach *(101)*
United States	1600	Chicago	Saltiene et al. *(97)*
Asia	5.5	Urban Bangkok	Wilcke et al. *(104)*
	55	Suburban Beijing	Wang et al. *(105)*
	317–154	Industrialized area, China	Ma et al. *(102)*

a mean carcinogenic PAH intake of 3.12 μg/day was estimated, of which dietary intake contributed 96.0%, air 1.6%, water 0.2% and soil 0.4% *(65)*. In the early 1990s, the potential dose of carcinogenic PAHs for American adult non-smoking males was estimated to be 3 μg/day up to a maximum of 15 μg/day. Smokers of unfiltered cigarettes might have had a potential dose twice that of non-smokers *(65)*.

Recent studies conducted on human exposure to B[*a*]P for non-smokers in developed countries revealed that nowadays, the range and magnitude of dietary exposures (0.5–320 ng/day) *(87)* are generally larger than for inhalation (0.15–26 ng/day). In certain cases where indoor air contains high concentrations of PAHs, however, air could be a major contributing source. This could be the case if a person spent the day in an ETS environment (4–62 ng/day) or in microenvironments fitted with non-airtight stoves (30–7448 ng/day)[7] or cooked food in the Chinese style (91–365 ng/day).[8]

[7] Calculated using the concentrations reported by Traynor et al. *(49)* and applying the USEPA *(67)* male individual's breathing rate.

[8] Calculated using the concentrations reported by Zhu & Wang *(41)* and applying the USEPA *(67)* male individual's breathing rate.

In developing countries where biomass is generally used for cooking in homes without a flue or with a deficient flue, the contribution of inhalation to the B[*a*]P exposure could be as high as 138–3320 ng/day[9] and therefore inhalation would be the main contributor to the total daily intake.

Indoor concentrations and their relation to outdoor concentrations

About 500 PAHs and related compounds have been detected in air, but most measurements have been made on B[*a*]P *(2)*. Indoor levels have been generally found to be influenced by seasonal variations, with higher levels in winter than in summer *(39,63)*. The levels of B[*a*]P in United States homes were found to be between 0.05 and 0.44 ng/m^3, which were within the range of B[*a*]P in European homes (0.01–0.65 ng/m^3) (as shown in Table 6.4). The highest B[*a*]P levels (0.09–25.52 ng/m^3) were found in Polish homes *(59)*.

The levels of B[*a*]P in Asian cities ranged between 0.21 and 3.4 ng/m^3 *(14,60–64)*. Higher levels of B[*a*]P were found in Chinese domestic kitchens. The average concentration of 12 PAHs[10] in Chinese domestic kitchens was 7.6 μg/m^3 and was dominated mainly by 3- and 4-ring PAHs. The B[*a*]P levels in domestic kitchens were 6–24 ng/m^3, which was associated with conventional Chinese cooking methods *(41)*. Lower concentrations were found in domestic kitchens in other Asian cities *(12,14,106)*.

The use of non-airtight stoves was found to increase the levels of B[*a*]P by up to 2–490 ng/m^3 *(49)*, while the mean indoor level of B[*a*]P in homes with airtight wood-burning stoves was 0.63 ng/m^3 *(49,50)*, which in turn is higher than those levels recorded in non-wood-burning homes *(34)*. High levels of B[*a*]P (70 ng/m^3) and other PAHs have been measured in traditional rural houses with unvented fireplaces in Burundi *(51)*.

High levels of 12 PAHs[11] (164.2 ng/m^3 geometric mean) have also been measured when kerosene stoves were used in Indian homes, with B[*a*]P geometric mean levels of 6.9 ng/m^3 *(37)*. However, the highest PAH levels were measured when using other solid fuels such as coal, wood and cattle dung, with B[*a*]P levels ranging from 33 to 166 ng/m^3. Homes in industrialized countries with ETS presented higher B[*a*]P levels (0.23–1.7 ng/m^3) than homes without the presence of ETS (0.01–0.58 ng/m^3) *(22,24,39,47)*.

The sum of all 16 gaseous and particle-bound PAHs measured in pubs, restaurants and discotheques varied between 22 and 840 ng/m^3 (B[*a*]P 1.45–4.1 ng/m^3)

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[9] Calculated using the concentrations reported by Raiyani et al. *(36,38)* and applying the USEPA *(67)* male individual's breathing rate.

[10] The 12 PAHs comprised naphthalene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benz[*a*]anthracene, chrysene, benzo[*k*]fluoranthene, benzo[*e*]pyrene and benzo[*a*]pyrene.

[11] The 12 PAHs comprised naphthalene, acenaphthylene, acenaphthene, fluorene, phenanthrene, anthracene, fluoranthene, pyrene, benz[*a*]anthracene, chrysene, benzo[*k*]fluoranthene and benzo[*a*]pyrene.

(39,40,107), with discotheques/clubs the locations with the highest mean concentrations in a study carried out in Germany *(40)*.

PAH concentrations measured in public indoor spaces ranged from 0.4–0.6 ng/m^3 in hospitals, libraries and coffee shops and 1.2–1.4 ng/m^3 in food courts and shopping malls in the United States *(108)* to 2.1–18.2 ng/m^3 inside Czech kindergartens *(109)*.

Indoor : outdoor ratios

The concentrations of low-molecular-weight PAHs (two and three rings) are usually higher indoors than outdoors, whereas those of high-molecular-weight PAHs (four rings and larger) are normally higher outdoors than indoors *(63)*, suggesting that the indoor concentrations of the high-molecular-weight PAHs are dominated by outdoor sources *(53)*. However, a study found that the 95th percentile of the I : O ratios of several four-ring PAHs were much higher than unity (> 3) *(53)*, suggesting than in some homes the influence of indoor sources (generally tobacco smoking, heating or cooking sources) may be considerable *(110)*.

The I : O ratios of individual PAHs varied from 0.3 to 10.5. Similarly, the I : O ratio of B[*a*]P ranged from 0.09 to 3.34 *(13,17,47,53,56,60–63,108,111)*. This variety in I : O concentration ratios suggest that the ratios fluctuate substantially across different settings, particularly those with smokers or indoor combustion sources and cooking activities *(61)*. The differences in I : O ratios are affected by variables such as differences in combustion sources and heating systems, climatic conditions and ventilation habits. Nevertheless, smoking is generally the most relevant factor in determining I : O ratios in homes in industrialized countries *(58)*.

Several studies found I : O ratios for PAH species of 1.4 ± 0.6 (B[*a*]P 1.6) in non-smokers' homes and much greater than unity (4.3 ± 3.3 for PAHs, B[*a*]P 5.5) in smokers' homes *(13,22,47)*.

The I : O levels in homes using kerosene stoves for cooking and heating were 4.5 for 12 PAHs (see footnote 11) and 7.6 for B[*a*]P. These high values for the I : O ratio show the impact of indoor combustion sources on indoor levels of PAHs *(37)*.

Toxicokinetics and metabolism

The kinetics and metabolism of PAH(s) have been addressed previously in several WHO documents *(2,8,70)*. The emphasis below is on aspects relevant particularly to exposure in indoor air. Moreover, the most recent data on PAHs are reviewed.

Identification of studies

Studies on pharmacokinetics, metabolism and toxicology were identified by hand searching references in former reviews by WHO (*2,8,70*) and other authors

(*112*) and by electronic searches in PubMed and the ISI Web of Science. As to the description of toxic effects, the focus was on in vivo studies but for the mechanisms of toxicity and metabolism all relevant studies were reviewed. Altogether, 320 original papers were selected from the literature searches with wide scope for review of contents, and 114 papers were included as relevant references for this work.

Toxicokinetics

Owing to differences in the physicochemical properties of PAHs, their toxicokinetics differ widely. In this section, the focus is on the kinetics of lipophilic high-molecular-weight PAHs, such as B[*a*]P, because they cause the main health concern.

Absorption

The major route of exposure to PAHs in the indoor environment is through the lungs and respiratory tract after inhalation of PAH-containing aerosols and particles. Data on the fate of PAHs in lungs are mainly based on animal and in vitro studies.

After deposition in the airways, the structure of the PAH and the dimensions and the chemical nature of the particles define the fate of the PAH. PAHs may dissolve from particles, the remainder in particles may be eliminated by bronchial mucociliary clearance of particles (to be swallowed), or the PAH in particles may remain in the lungs for a longer time.

B[*a*]P is rapidly absorbed in the lungs from solutions. After intratracheal instillation of radiolabelled B[*a*]P in rats, the peak concentration in the liver was attained in 10 minutes *(113)*. The B[*a*]P-associated radioactivity was cleared from lungs with elimination half-lives of 5 and 116 minutes, respectively.

PAH in particles follows biphasic absorption kinetics in the lungs. The absorption kinetics depends on the site of deposition in the respiratory tract. A fraction of B[*a*]P in diesel particles was quickly desorbed and absorbed into circulation through type I epithelial cells in the alveolar region *(114–116)* and systemically rapidly metabolized *(116)*. The fraction deposited in the tracheobronchial region was more slowly absorbed into circulation and intensely locally metabolized *(116)*. The release rates of B[*a*]P from particles decreased drastically after the initial burst and a notable fraction of B[*a*]P (up to 30%) remained unaffected on the surface of particles in lungs and in lymph nodes for several months *(116)*.

In perfused rat lung, the absorption kinetics of B[*a*]P is dose-dependent *(117)*. At low exposure levels, absorption of B[*a*]P in the mucosa followed the first-order kinetics with substantial local metabolism. At high exposure levels, the capacity of epithelium to dissolve and metabolize B[*a*]P became saturated and the absorption rate turned constant (zero-order kinetics). In the indoor environment, human exposure most likely follows the low-dose, first-order kinetics.

No data are available on exact quantitative estimates of PAH absorption in human lungs.

The kinetics of lipophilic PAHs in lungs suggest that, after deposition in lungs, (*a*) there is a rapid systemic exposure to B[*a*]P after inhalation of PAH-containing particles, (*b*) the intracellular B[*a*]P is higher in the tracheobronchial region than the alveolar region and in the epithelium lining the airways, and (*c*) there is a sink of B[*a*]P in particles to cause long-term exposure in lungs and local lymph nodes after inhalation exposure.

B[*a*]P and other PAHs (phenanthrene and pyrene) efficiently penetrate the skin in animals. Absorption of up to 84% of the B[*a*]P-associated radioactivity has been observed in mice *(118)* and 46% in rats *(119)*. Absorption through human skin may be less efficient than in animals.

PAHs are ingested in house dust (as a non-dietary source) and swallowed in particles that are transported by mucociliary transport from the lungs. PAHs are readily absorbed in the gastrointestinal tract by passive diffusion *(120)*. The composition of the diet may increase or decrease the absorption *(8)*. Bioavailability from particles limits the absorption. From soil particles, up to 50% of total PAHs was absorbed from the gastrointestinal tract in vitro *(121)*. The absorption was highest for small-molecule PAHs (naphthalene, acenaphthene, anthracene). The bioavailability from particles, however, probably varies depending on the content of organic carbon in dust particles.

Distribution

PAHs are rapidly and widely distributed in the body. Lipophilic compounds easily pass biological membranes. Detectable levels of B[*a*]P can be observed in most tissues in minutes to hours after exposure, irrespective of the exposure route. PAHs undergo hepatobiliary clearance *(122)* and high concentrations of PAHs and their metabolites are detectable in the gastrointestinal tract *(8,122)*.

PAHs do not accumulate in the body. Fat tends to contain more PAHs than other tissues *(8)*. Fat and PAH contents, however, did not correlate well in lungs *(123)*.

PAHs are generally detectable in most human tissues, typically at the sub-μg/kg level *(8)*. The reactive metabolites are bound covalently to proteins and nucleic acids and the turnover rate of adducts defines the half-life in tissues.

Particles may cause high concentrations of PAHs in lungs. A 100-fold higher radioactivity occurred in lungs of rats after inhalation of labelled B[*a*]P adsorbed on carbon black particles than after inhalation of pure B[*a*]P. The half-time of decline also lengthened from 6 weeks to 34 weeks *(124)*.

B[*a*]P and other PAHs can readily cross the placental barrier *(8)*. The concentrations in animal embryo tissues have been, however, at one to two orders of magnitude lower than in maternal organs *(125–127)*. PAHs, including B[*a*]P, are detectable in maternal milk *(128)*.

Excretion

The faeces are the main route of excretion of high-molecular-weight PAHs and their metabolites *(8)*. Biliary secretion and enterohepatic circulation are significant *(122,129)* and increase the concentrations of metabolites and parent compounds in the gastrointestinal tract. PAHs in bile are nearly completely present as metabolites. Less than 1% was detected as B[*a*]P in bile after intravenous administration of B[*a*]P to mice *(122)*.

Urine is the other main excretion route. Some 4–12 % of B[*a*]P was excreted in urine in rats *(122)* compared with 60% of pyrene as metabolites *(130)*. The role of urine as an excretion route is compound-specific; for large-molecule PAHs, it is a minor route.

Metabolism

Metabolism is crucial for toxicity of PAHs. Reactive intermediates and metabolites are formed that cause the toxicity and carcinogenicity. The metabolism pathways of B[*a*]P are best known *(2,8,70,112)*. Most other large-molecule PAHs probably follow the same metabolism patterns *(131)* but the metabolic activation of sterically nonalternant PAHs, such as benzo[*b*]fluoranthene, may differ *(2)*.

Three principal pathways activate PAHs for toxic intermediates and further metabolism: that via (dihydro)diol-epoxide formation, that via radical cation formation, and the *o*-quinone pathway *(112,131)*. Several enzymes interplay in the metabolism.

The key enzymes in PAH metabolism are CYPs (cytochrome P450s) and epoxide hydrolase. CYPs activate PAH to optically active oxides, which rearrange to phenols. Epoxide hydrolase converts the oxides (epoxides) to optically active dihydrodiols (diols) *(8,112)*. CYPs also metabolize PAHs to a series of quinones. For B[*a*]P, three quinones have been identified in vitro and in vivo: B[*a*]P-1,6-quinone, B[*a*]P-3,6-quinone and B[*a*]P-6,12-quinone *(132)*. The diols can be converted to four optically active isoforms of diol-epoxides by CYPs. The diol-epoxides are highly reactive towards DNA and form a series of stable DNA adducts *(112)*. The (+)-*anti*-B[*a*]P-7,8-diol-9,10-epoxide (*anti*-B[*a*]PDE) is suggested to be the ultimate carcinogenic form of B[*a*]P *(112,131)*.

The catalytic property, mode of regulation and tissue specificity of CYPs vary and there are species differences. One or more members of the CYP family are capable of metabolizing one or more PAHs. The highest metabolism capacity is in the liver, followed by the lung, intestinal mucosa, skin and kidneys *(8)*. Toxic metabolites producing CYPs are expressed and induced in a number of other tissues, including cardiovascular tissues *(133,134)*. The key enzymes for PAH metabolism are CYP1A1 and CYP1B1 but several other CYPs (CYP1A2, CYP2B, CYP2C and CYP3A) also metabolize PAHs *(8,112)*.

PAHs, especially B[*a*]P *(135)*, stimulate their own metabolism by inducing CYP enzymes *(8)*. CYP1A and CYP1B are induced via the Ah-receptor *(8)*. En-

zyme induction results in lower tissue levels of PAHs and more rapid excretion of PAHs as metabolites.

The site of induction is important for toxicity. Strong induction of the metabolism in the liver decreases PAH levels in peripheral tissues and levels of toxic metabolites by local CYP metabolism. Clear differences in PAH toxicity have been demonstrated in mice strains of different CYP induction capacity *(8,136–138)*. PAHs also inhibit CYP enzymes, and even their own metabolism *(139)*. On the basis of toxicokinetics, PAHs may be expected to be relatively more toxic through inhalation and dermal exposure (owing to focal toxicity at the site of entry) than after oral exposure, because inhalation and dermal exposure bypass the first-pass metabolism in the liver.

The diol-epoxides have been regarded as principal toxic metabolites *(70)* but recent data suggest that two other routes of PAH metabolism produce toxic metabolites. In the radical cation metabolism pathway, radical cations are formed from PAH by CYPs or peroxidases and these form depurinating DNA adducts *(140)*. In the *o*-quinone pathway, *o*-PAH diols are converted by aldo-keto reductases to catechols, which autoxidize to *o*-quinones. These *o*-quinones undergo redox cycling and form reactive oxygen species *(131,141)*. Other B[*a*]P quinones have also been associated with reactive oxygen species and mutagenesis. In vivo, both mice and rats metabolize B[*a*]P to B[*a*]P-1,6-quinone, B[*a*]P-3,6-quinone and B[*a*]P-6,12-quinone and these quinones redox cycle and induce mutations *(132,142)*. Reactive oxygen species have been associated with carcinogenesis *(131,141)*.

Although B[*a*]P-diol epoxides, B[*a*]P-radical cations and B[*a*]P-*o*-quinones can form DNA adducts in vitro, only B[*a*]P-diol epoxide- and B[*a*]P-depurinating-DNA adducts have been measured in vivo in experimental animals and in humans *(131,140,143,144)*. The relative importance of each activation pathway of metabolism depends on several factors, including the tissue level and stability of each activated form and the levels of expression of the activation and detoxification enzymes. For B[*a*]P, based on the wealth of data, the diol epoxide metabolic activation mechanism seems to be the dominant mechanism in the induction of lung carcinogenesis in rodents and humans. This conclusion is based on toxicological and mechanistic data obtained from experimental animals and from the many human biomarker studies.

PAHs and their reactive metabolites are finally converted to more polar and detoxified metabolites for excretion by the phase II metabolism enzymes, including glutathione *S*-transferase, UDP-glucuronosyltransferase, sulfotransferase, NAD(P)H-quinone oxidoreductase 1 and aldo-keto reductase *(112)*. Though some of them may also be induced by PAHs, the induction is not as strong as CYP induction *(145)*.

Genetic polymorphism may contribute to capacity to metabolize PAHs and affect toxicity. Genetic polymorphism has been described in CYP1A1, CYP1A2,

CYP1B1, some CYP2C and CYP3A *(8)* and phase II detoxification enzymes *(112,146)*.

Metabolism in the respiratory tract has particular relevance for toxicity of inhaled PAHs. Macrophages are actively metabolizing cells of PAHs in the lung *(8)*. Macrophages can engulf PAH-containing particles and transport them to bronchi. It has been hypothesized that ultimate carcinogenic metabolites released from macrophages contribute to cancer development in the lung *(8)*.

Health effects

DNA adducts

The formation of DNA adducts is a key event in mutagenicity and carcinogenicity by PAHs. Owing to the many stereoisomeric forms of B[*a*]P-diol epoxides (BPDE), their reactivity to covalently bind to nitrogen atoms on guanine (and to a lesser extent on adenine) bases, and epoxide ring opening yielding both *cis* and *trans* adducts, a potential total of eight unique B[*a*]P-diol epoxide stereoisomeric DNA adducts can be formed for each site on the nucleic acid base *(131)*. However, far fewer stable DNA adducts are observed in vitro or in vivo. Only one diol epoxide B[*a*]P-DNA adduct (anti-B[*a*]PDE-deoxyguanosine) was observed in the lungs of mice treated with B[*a*]P *(147)* and the same adduct was found in human diploid lung fibroblasts in vitro *(148)* and in mononuclear white blood cells from exposed coke oven workers *(149)*.

In heavily PAH-exposed workers, the anti-B[*a*]PDE-DNA adducts in peripheral blood lymphocytes were associated with increased micronuclei in cells *(150)*. Radical cations produce a series of B[*a*]P adducts on guanine and adenine that are unstable (depurinating) and cleave from the DNA *(131,140)*. *o*-Quinones, another metabolite of B[*a*]P, also form both stable and unstable adducts in vitro *(131,144)*. PAH-DNA adduct formation blocks DNA replication and induces base and nucleotide excision repair activities *(151)*. Errors in DNA replication (misreplication) and in DNA repair (misrepair) can create mutations that are fixed after cell division.

DNA adducts display tissue- and compound-specific qualitative and quantitative differences *(152,153)*. B[*a*]P formed DNA adducts in rat lungs and liver in a dose- and time-dependent way *(153)*. In rats and mice, the adducts reach maximal levels in tissues within a few days after a single dose, after which they gradually decrease but persist for several weeks *(147,154–156)*. In the rat lung, two adducts predominated equally (adduct with B[*a*]P-diol epoxide and 9-OH-B[*a*]P-derived adduct, about 40% of each) after intraperitoneal administration in the liver, the B[*a*]P-diol epoxide adduct dominated. These same adducts have also been detected in the lungs of mice, B[*a*]P-diol epoxide predominating *(157)*. A comparative study with different PAHs in A/J mice indicated that the formation and persistence of DNA adducts determined the potency to induce adenomas in lungs after a single intraperitoneal administration *(147)*.

DNA adducts have been observed postnatally in thymocytes and splenocytes of pups after in utero exposure of mice to B[*a*]P *(158)*, indicating rather long persistence of the DNA adducts and vulnerability of pups to gestational exposure to B[*a*]P. PAH-DNA adducts have been detected in human fetal umbilical cord blood and maternal blood after exposure to ambient air PAHs at different levels *(159)*. Prenatal exposure may increase the cancer risk of PAHs.

Mutagenicity

A number of PAHs are mutagenic and genotoxic, and induce DNA adduct formation in vitro and in vivo *(8)*.

The potential to cause mutations is compound-dependent. Dibenzo[*a,l*]pyrene-diol-epoxide was over 60-fold more reactive towards DNA, induced over 200 times more mutations and yielded a fourfold higher yield of mutations per adduct than B[*a*]P-diol-epoxide in V79-derived XEM2 cells *(160)*. Moreover, dibenzo[*a,l*]pyrene-diol-epoxide-induced adducts were less efficiently repaired.

Some PAHs probably cause mutations in a number of genes that contribute to cancer development. The *anti*-diol-epoxide of B[*a*]P ((±)-*anti*-BPDE) causes adducts at several hotspots of the *p53* gene *(161)*, especially in codons 157, 248 and 273 *(162)*. The mutations by this epoxide are predominantly G to T transversions *(163,164)*. Diol epoxides of several other PAHs cause adducts in these and other codons *(165)*. PAH *o*-quinones have more potently caused similar *p53* mutations in yeast reporter gene assay than (±) *anti*-BPDE *(161)*. PAH-induced DNA damage stimulates cellular p53 accumulation and up-regulates the p21 protein *(148,166)* as typical cellular responses to DNA damage. In experimental animals, tumours induced by a series of PAHs have harboured mutations in K-*ras* (lung tumours) and H-*ras* oncogenes (skin, liver and mammary tumours). B[*a*]P has induced K-*ras* codon 12 mutations in mouse lung tumours almost exclusively at guanine, consistent with the detection of *anti*-BPDE-deoxyguanosine-DNA adducts in the lung tissues *(167)*.

In human studies, lung tumours from non-smokers exposed to PAH-rich coal combustion emissions had mutations at guanine in K-*ras* codon 12 and *p53* genes *(168)*.

In addition to base-pair substitutions, PAHs cause other mutations to a lesser extent (exon deletions, frame-shift mutations) *(163,169)*.

Ambient air particles have variably caused genotoxicity in vitro and DNA adduct formation *(170,171)*. PAHs, especially B[*a*]P *(170,172)* and nitro- and oxy-PAHs, are major active components *(171)*. B[*a*]P levels have indicated well the presence in ambient air of compounds causing DNA adducts *(172)*.

In a limited data set, PAHs were assessed to contribute 3–23% of the mutagenicity in settled house dust *(173)*. On the mass basis, settled house dust was considered on average more mutagenic than contaminated soils but less mutagenic than suspended particles in indoor and outdoor air *(173)*.

Because some PAHs cause mutations and genotoxicity, they may generally be regarded as genotoxic carcinogens. However, PAHs also promote tumour development (see below).

Carcinogenicity

B[*a*]P and a number of 4- to 7-ring PAHs are carcinogenic in experimental animals *(8,70)*. Several small-molecule PAHs, such as anthracene, perylene and fluorene, have not been carcinogenic and the carcinogenicity of some compounds (acenaphthene, phenanthrene, pyrene) is, as yet, questionable *(8)*. Inhalation of naphthalene has induced respiratory tract tumours in mice and rats at high cytotoxic concentrations but not at non-cytotoxic concentrations *(174,175)*.

Carcinogenic PAHs such as B[*a*]P have induced tumours through dermal, oral, intraperitoneal, intramamillary and respiratory tract routes *(8)*. The species that have developed tumours after exposure to PAHs include mice, rats, rabbits, hamsters and monkeys *(8)*. Tumour induction is not restricted to the site of administration. After oral exposure to PAHs, tumours have been observed typically in the liver, forestomach, lungs and mammary glands *(8)*. PAHs painted onto skin have caused skin papillomas and carcinomas but also lung and liver tumours *(8,70)*. Administration of B[*a*]P into the respiratory tract has consistently caused lung tumours in mice, rats, hamsters and monkeys *(8)*. Fewer data exist for other PAHs after exposure via the respiratory tract, but acenapthene, benzo[*b*]fluoranthene, benzo[*j*]fluoranthene, benzo[*k*]fluoranthene, chrysene, dibenz[*a,h*]anthracene and indeno[*1,2,3-c,d*]pyrene have caused lung tumours in rats and dibenz[*a,h*]anthracene and dibenzo[*a,i*]pyrene in hamsters *(8)*.

The potencies of the carcinogenic PAHs differ by three orders of magnitude *(8)*. In comparative studies with PAHs, B[*a*]P was repeatedly a potent carcinogen after dermal application *(8)* but in an initiation–promotion model in SENCAR mice, dibenzo[*a,l*]pyrene and 7,12-dimethyl-benz[*a*]anthracene were more potent initiators of skin tumorigenesis than B[*a*]P *(176,177)*. Based on the administered dose, dibenzo[*a,l*]pyrene was also more potent than B[*a*]P in inducing mouse lung adenomas *(178)*. Since dibenzo[*a,l*]pyrene was also the most potent in inducing mammary tumours after intramamillary injection *(176)*, it may be regarded as the most potent carcinogenic PAH known.

B[*a*]P *(8)* and dibenzo[*a,l*]pyrene *(179,180)* have been shown to be transplacental carcinogens in mice, causing lung and liver tumours (B[*a*]P and dibenzo[*a,l*]pyrene) and lymphoma (dibenzo[*a,l*]pyrene) in progeny after in utero exposure.

Limited data are available on the potency of specific PAHs to induce lung cancer following inhalation exposure. Data are inadequate for ranking the potency of specific PAHs to induce lung cancer.

The Ah-receptor-mediated pathways are crucial for carcinogenicity of PAHs: Ah-receptor-deficient mice are resistant to B[*a*]P- and dibenzo[*a,l*]pyrene-

induced skin cancer *(181,182)*. Organic extracts of airborne particulate matter, where PAHs are suggested to be the primary carcinogens, have not caused lung tumours in AhR -/- mice either *(183)*.

Although genotoxic effects (mutations in cancer genes and DNA damage) are likely to be the primary events in PAH-induced carcinogenesis, in vitro studies have indicated that PAHs have also non-genotoxic effects that could contribute to carcinogenesis. B[*a*]P-diol epoxide induces gene promoter hypermethylation in immortalized bronchial epithelial cells *(184)* and several PAHs inhibit gap-junctional intercellular communication *(185)*, a typical mechanism of tumour promotion. Several small-molecule PAHs have been more potent in inhibiting gap-junctional intercellular communication in liver cells than high-molecular-weight PAHs *(185)*. *Anti*-B[*a*]P-7,8-diol-9,10-oxide has been shown to increase cell proliferation in human cell lines, including lung cancer cells *(186)* and to induce apoptosis in H460 human lung cancer cells *(187)*. B[*a*]P has induced apoptosis in human lung fibroblast MRC-5 cells via the JNK1/FasL and JNK1/p53 signals *(188)*. It is possible that PAHs with low genotoxic potential also promote tumour development by non-genotoxic mechanisms.

PAHs have induced the expression of a number of genes in cells in vitro with compound-specific profiles *(189–191)*. Little can be interpreted as yet, however, about the mechanisms of toxicity from the gene and protein expression data. In addition to induction of PAH-metabolizing CYP genes, only oxidative stress pathway genes were induced by carcinogenic PAHs in rat liver slices *(190)*. In human mammary carcinoma-derived cells (MCF-7), cytoskeletal proteins, heat-shock proteins, DNA-associated proteins and glycolytic and mitochondrial proteins were altered *(191)*. Dibenzo[*a,l*]pyrene and B[*a*]P, two potent carcinogenic PAHs, have consistently displayed different gene expression patterns *(189–191)*. Diol epoxides of carcinogenic PAHs, but not the parent PAHs, have increased intracellular Ca^{2+} in human small-airway epithelial cells in vitro *(192)*. Increased intracellular Ca^{2+} is likely to be one mechanism contributing to the toxicity of diol epoxides.

General toxicity

There are limited data on the toxicity of individual PAHs in experimental animals. Data on mixtures containing PAHs as principal toxic components (coal tar, coal tar pitch and creosote) complement the information. In general, the acute toxicity of PAHs in animals is low to moderate *(8)*. B[*a*]P causes eye irritation and skin sensitization in animals *(8)* and PAH mixtures are phototoxic in both skin and eyes *(193)*.

On repeated exposure, the main target organs of toxicity are the liver or kidneys in animals, depending on the PAH *(8)*. Typically, the weight of the liver increases owing to enzyme induction. Nephropathy and decreased kidney weight have been caused by pyrene in mice *(8)*.

High oral doses of B[*a*]P have caused bone marrow depression in mice, decreasing especially proliferating haematopoietic cells *(137)*. B[*a*]P has also impaired in vitro proliferation and differentiation of human haematopoietic CD34+ stem cells and caused their apoptosis *(194)*. By destroying these cells, PAHs may down-regulate cell lineages (lymphocytes, macrophages, neutrophils) important for immunoresponse.

PAHs are immunotoxic and cause immunosuppression. Immunotoxicity of PAHs has been demonstrated in several different cells in vitro *(194–197)*. Immunotoxicity requires focal PAH metabolic activation in cells *(194,197)*. Immunosuppression in B6C3F1 mice has followed the structure–activity relationship observed for the carcinogenicity of PAHs, with benz[*a*]anthracene, B[*a*]P, dibenz[*a,c*]anthracene and dibenz[*a,h*]anthracene being more potent than anthracene, chrysene, benzo[*e*]pyrene and perylene *(136)*. The greatest immunosuppression was observed with 3-methylcholanthrene and 7,12-dimethylbenz[*a*] anthracene.

PAHs, including B[*a*]P, dibenz[*a,h*]anthracene, dibenz[*a,c*]anthracene and 7,12-dimethylbenz[a]anthracene, have accelerated atherosclerosis plaque formation in Ah-responsive mice, chickens and pigeons *(198,199)*. The atherogenic effect of PAHs may not be associated with their mutagenic and carcinogenic capacity *(200)*. PAHs are thought to cause adverse cardiovascular effects by metabolites through activation of the Ah-receptor: by increased production of reactive oxygen species, induction of inflammatory-mediated *(201)* and hypertrophic genes, and increased disruption of endogenous substances such as prostaglandins *(134)*. Therefore, induction of inflammation might be a crucial process in PAH-enhanced atherogenesis.

B[*a*]P has decreased fertility and caused embryotoxicity. It increased primordial oocyte destruction, decreased the number of corpora lutea, caused resorptions, decreased the number of pups and decreased fetal weight in rats and mice *(8)*. Sterility associated with alterations in gonadal tissues has also been observed in mice after prenatal exposure, in both females and males *(202)*. In male rats, B[*a*]P reduced testis weight *(203)* and decreased the testosterone level in the blood and sperm motility *(203,204)*, probably contributing to reproduction toxicity.

PAHs are also teratogenic in mice and rats *(8,205)*. Reproduction toxicity has also been noted by the dermal and parenteral exposure routes. Inhalation exposure of rats to B[*a*]P during pregnancy decreased plasma estrogen, progesterone and prolactin levels in dams in association with decreased pup survival and development, thus partly explaining the effects *(206)*. B[*a*]P exposure before conception caused Ah-receptor-dependent fetal intrauterine growth restriction in mice, which was associated with altered vasculature in the placenta and a decreased placental cell death rate *(207)*. Maternally toxic doses of B[*a*]P and 7,12-dimethylbenz[*a*]anthracene caused necrosis in the placenta and haemor-

rhages in fetuses in rats *(208)*, suggesting that the vascular system in general is one target of PAHs.

B[*a*]P, benz[*a*]anthracene and fluoranthene displayed weak estrogenic activity in rat immature uterotropic assay *(209)*, with 3–4 orders of magnitude lower potency than endogenous estrogen. Some PAHs (including B[*a*]P), and especially their hydroxylated metabolites, interact with estrogen receptors *(210,211)*. PAHs have also indicated anti-estrogenic effects *(212)*. Contrasting effects may be explained by a complex crosstalk between Ah-receptor and estrogen receptors and induction of estrogen metabolism by PAHs *(209)*.

PAH mixtures

In indoor air, exposure to PAHs occurs mostly in mixture. Since the toxicity of PAHs depends nearly exclusively on their biotransformation to toxic metabolites, interactions at the level of key metabolism enzymes are highly relevant to the associated health risk. Induction of metabolism by one PAH may enhance the toxicity of another; inhibition of the metabolism may decrease the toxicity.

Gene expression data with B[*a*]P and dibenzo[*a,h*]anthracene in binary mixture with dibenzo[*a,l*]pyrene, benzo[*b*]fluoranthene and fluoranthene in precision-cut rat liver slices in vitro indicated that (*a*) each of them induced an altered expression of genes, (*b*) the genes affected considerably by the combination of PAHs were slightly different from those altered by either of the constituents, (*c*) total altered expression of the genes by a mixture was less than that induced by individual PAHs and (*d*) the interactions were mostly antagonistic, leading to decreased altered expression of genes by the mixture compared to single PAHs *(213)*. Fewer DNA adducts were formed by the mixtures than by individual PAHs. In contrast, in human hepatoma cells (HepG2), equimolar and equitoxic mixtures of these same PAHs have shown an additive effect on apoptosis and cell cycle blockage, an additive or antagonistic effect on gene expression, and a synergistic effect on DNA adduct formation *(214)*. Since the interactions depend on PAH composition, concentrations and cell types, contrasting results may be expected. However, the majority of in vitro studies have shown an antagonistic effect on DNA adduct formation by a mixture of PAHs *(172,189,215)*.

The PAH metabolites have been shown to interfere with each other. The major B[*a*]P metabolite 3-hydroxybenzo(*a*)pyrene inhibits both the mutagenic and tumorigenic activity of the carcinogenic metabolite *anti*-B[*a*]PDE *(216)*. When applied topically to mouse skin, different binary and tertiary mixtures of carcinogenic PAHs formed DNA adducts at levels that were additive, less than additive and greater than additive relative to the levels formed when the compounds were applied individually *(217)*. Complex PAH mixtures have also decreased skin tumorigenicity of B[*a*]P *(218)* and that of dibenzo[*a,l*]pyrene in mice *(219)*. Decreased tumorigenesis was associated with decreased DNA adduct formation. In contrast, mixtures of five PAHs both enhanced and inhibited mouse lung tu-

morigenesis, depending on the composition of the PAH mixture and the dose *(220)*.

Altogether, the experimental data indicate that mixture effects of PAHs may be complex in vitro and in vivo. Attenuation of the toxicity rather than synergism has been observed in several studies. These observations imply that the effects of a PAH mixture may not be reliably predicted from single PAH components.

Biomarkers for evaluation of exposure

Internal exposure to PAHs has been assessed mostly by urine 1-hydroxypyrene or aromatic bulky DNA adducts in peripheral lymphocytes in humans *(8)*.

1-Hydroxypyrene, a metabolite of non-carcinogenic pyrene detectable in urine, may be used as a general biomarker of exposure to PAH mixtures *(8,221)*. Because urinary 1-hydroxypyrene displays all possible sources of PAHs (including food and ambient air) and all exposure routes, it indicates total exposure to pyrene-containing PAH mixtures. A good correlation between the PAH concentration in air and urine 1-hydroxypyrene has been observed in several occupational environments *(8)*. In single studies, a significant correlation has also been observed with exposure to residential indoor air sources of PAHs, such as ETS, cooking practices and the burning of coal for heating *(222,223)*. A review on environmental exposure to PAHs in ambient air indicated that urine 1-hydroxypyrene may serve as a qualitative indicator of excess exposure to PAHs at the group level but a large inter-individual variation limits its use for personal exposure *(224)*.

The levels of DNA adducts reflect not only the exposure to PAHs but also the body's ability to metabolize them. In general, exposures that have led to increased excretion of 1-hydroxypyrene have led to elevated adduct levels *(8)*. This is demonstrated best on occupational exposure to PAHs. However, the inter-individual variation in DNA adducts has been large (up to 50–100-fold) and the correlation between measured/estimated exposure to PAHs and adduct levels variable (from clear to no correlation, for example *(225)*). The correlation may be better when exposure is measured personally *(226)*. As to the general population, elevated DNA adduct levels in blood leucocytes have been detected in populations living in industrialized areas *(227–229)*. Consumption of charcoal-grilled food increases their levels *(230,231)*, as does high indoor air exposure *(232)*. Total PAH-DNA adduct levels and BPDE-DNA adduct levels were significantly higher in smokers than among non-smokers *(233)*. Altogether, PAH-DNA adducts can be used as a qualitative biomarker of exposure to combustion emissions, most reliably on a group basis. DNA adducts are considered to be a less sensitive parameter for exposure assessment than excretion of 1-hydroxypyrene in urine *(8,224)*.

Environmental exposure to PAHs may not be assessed reliably on the basis of exposure biomarkers such as urinary 1-hydroxypyrene concentration or aro-

matic bulky PAH-DNA adducts in blood cells. This is particularly true in indoor environments, where assessment at individual level is often needed. There are no proper risk functions, the individual variation in biomarkers is large and the biomarkers measure exposure to all possible sources of PAHs (including ambient air and food).

Human health effects

While the risks of occupational exposure to PAHs are not the focus of this chapter, indoor exposure to smoke from biomass and coal burning for the population in developing countries could be comparable to the levels of pollutants in the occupational setting *(234)*. For example, indoor particulate matter (< 10 μm) levels in solid-fuel-burning households reach up to several milligrams per cubic metre. An estimated half of the global population depends on solid fuel for cooking and heating, often in inadequately ventilated spaces *(234)*. Women and children are particularly vulnerable because of the longer time spent at home. Timing of exposure in children could influence disease risk owing to the sensitive window of development, as well as exposure levels that are often higher relative to their body size. Indoor smoke exposure in such settings remains one of the top ten risks in the global burden of disease *(235)*.

Identification of studies

PubMed was searched in English, the search being restricting to human studies. For non-carcinogenic effects, the following search terms were used: "polycyclic aromatic hydrocarbons AND indoor AND birth weight", "polycyclic aromatic hydrocarbons AND smoke", "polycyclic aromatic hydrocarbons AND biomass", "polycyclic aromatic hydrocarbons AND coal burning", "polycyclic aromatic hydrocarbons AND indoor AND intrauterine growth restriction", "polycyclic aromatic hydrocarbons AND indoor AND low birth weight", "polycyclic aromatic hydrocarbons AND indoor AND small-for-gestational age", "polycyclic aromatic hydrocarbons AND indoor AND birth length", "polycyclic aromatic hydrocarbons AND indoor AND birth head circumference", "polycyclic aromatic hydrocarbons AND indoor AND fetal growth", "polycyclic aromatic hydrocarbons AND indoor AND neurodevelopment", "polycyclic aromatic hydrocarbons AND indoor AND PAH-DNA adducts", "polycyclic aromatic hydrocarbons AND indoor AND bronchitis" and "polycyclic aromatic hydrocarbons AND indoor AND asthma".

For carcinogenic risk, the following search terms were used: "polycyclic aromatic hydrocarbons AND 1-hydroxypyrene", "polycyclic aromatic hydrocarbons AND PAH-DNA adducts", "polycyclic aromatic hydrocarbons AND DNA", "polycyclic aromatic hydrocarbons AND chromosom*", "polycyclic aromatic hydrocarbons AND cancer", "polycyclic aromatic hydrocarbons AND occupational", "polycyclic aromatic hydrocarbons AND ischaemic heart disease", "poly-

cyclic aromatic hydrocarbons AND cognitive" and "polycyclic aromatic hydrocarbons AND neurodevelopment*".

The search identified 455 papers. Moderate to large population-based prospective cohort studies using a quantitative assessment of PAH exposure were given first priority. Studies that did not adjust for known and potential confounders were not considered. Clinical trials, risk assessments, reviews of the literature, future studies, case reports, diagnostic guidelines and studies that lacked quantitative assessment of exposure were also excluded from the review. Subsequently, 178 papers were chosen for full review and 56 papers are included in the present report. In addition, earlier reviews by WHO *(2,8)*, IARC *(70,92,260)* and other authors *(130)* were considered.

Non-carcinogenic effects

Intrauterine growth restriction. Intrauterine growth restriction has been operationalized as low birth weight (< 2500 g), low birth weight at full term and small for gestational age (SGA), defined as < 10th percentile of population mean weight at a given gestational age and gender.

Prenatal exposure to PAHs has been associated with reduction in birth weight, an increased likelihood of low birth weight in Europe and the United States *(236)* and SGA *(237,238)* in a dose-responsive manner, after controlling for region- and cohort-specific sets of confounders. In Teplice and Prague (Czech Republic), PAHs isolated from respirable particulate matter during winter induced the highest genotoxicity and embryotoxicity *(239)*. High ambient concentrations of PAHs, PM_{10} and $PM_{2.5}$ during the first month of gestation were associated with a significantly elevated risk of SGA in the industrial city of Teplice *(237)*. A study in Poland showed that neonates with high levels of PAH-DNA adducts in the leucocytes had significantly lower birth weight, length and head circumference *(240)*.

Two parallel prospective cohort studies in Krakow and New York City enrolled non-smoking pregnant women with no known risks of adverse birth outcomes and monitored their personal PAH exposure concentrations *(241)*. Mean personal PAH exposures to eight carcinogenic PAHs[12] differed more than 10-fold between the two cities (Krakow mean 39.0 ng/m^3, range 1.8–272.2 ng/m^3; New York mean 3.3 ng/m^3, range 0.3–36.5 ng/m^3). In the Krakow cohort, prenatal exposure to the summed eight carcinogenic PAHs was significantly associated with reduced birth weight (68.75 g),[13] birth length (0.48 cm) and birth head circumference (0.21 cm) *(241)*. In the New York cohort, however, prenatal exposure to PAHs was associated with reduced birth weight (177.57 g) among New York African Americans but not among New York Dominicans *(241)*. Furthermore, a natural log-unit in-

[12] Sum of benz[*a*]anthracene, chrysene/isochrysene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, B[*a*]P, indeno[*1,2,3-c,d*]pyrene, dibenz[*a,h*]anthracene and benzo[*g,h,i*]perylene.

[13] Per natural-log unit of the carcinogenic PAHs.

crease in prenatal PAH exposure was associated with a two-fold increase in the likelihood of being born SGA among African Americans but not Dominicans in New York *(238)*. SGA is one of the most clinically predictive markers of fetal growth impairment. SGA has been associated with a significantly greater risk of delayed neurodevelopment *(242,243)*, shorter stature, cardiovascular disease, insulin resistance and diabetes during adulthood *(244,245)*. Among the New York African Americans, a natural log-unit of prenatal exposure to PAHs[14] was associated with a five-fold greater risk of preterm delivery (< 37 weeks at birth) *(238)*. While residual confounding remains a possible alternative explanation, African American neonates and children appear to be more vulnerable.

Bronchitis, asthma and asthma-like symptoms. In the same New York City cohort, prenatal exposure to the particle-bound PAHs may increase the risk of asthma symptoms by the age of 1–2 years *(246)*. In Teplice and Prachatice in the Czech Republic, unit exposure to ambient 100 ng/m^3 PAHs, based on a 30-day average, and a unit exposure to 25 μg/m^3 $PM_{2.5}$ were respectively associated with 56% (95% CI 22–100) and 23% (95% CI –6 to –62) increases in the risk of bronchitis in children between the ages of 2 and 4½ years *(247)*.

Fatal ischemic heart disease. A multinational cohort of male asphalt workers was followed for fatal ischemic heart disease (IHD) for 17 years (SD = 9 years). Mean personal exposure to B[*a*]P for the cohort was 273 ng/m^3. For those exposed to ≥ 273 ng/m^3 B[*a*]P, the risk of IHD mortality was 1.64-fold greater (95% CI 1.13–2.38) than in those exposed to ≤ 68 ng/m^3 *(248)*. The risk increased in a dose-responsive manner. At the highest PAH exposure category, cigarette smoking by the workers did not explain the significant increase in IHD mortality risk, thus supporting the etiological role of B[*a*]P.

Neurodevelopmental index

In the same New York City birth cohort, those neonates with a higher than median prenatal PAH exposure (range 4.16–36.47 ng/m^3) had a significantly lower Bayley Mental Development Index as well as a greater likelihood of cognitive developmental delay at the age of three years compared to children exposed to 0.27–4.15 ng/m^3, controlling for ethnic background, gender, gestational age, level of nurturing provided at home, ETS and chlorpyrifos exposure *(249)*.

In a cross-sectional investigation in Tongliang, China, babies born close to a coal-fired power plant in 2002 were associated with 0.32 ± 0.14 B[*a*]P DNA adducts per 10^8 nucleotides *(250)*. Such a level of B[*a*]P adducts at birth was associated with a decreased motor development quotient at two years of age *(250)*. A

[14] Sum of benz[*a*]anthracene, chrysene/isochrysene, benzo[*b*]fluoranthene, benzo[*k*]fluoranthene, B[*a*]P, indeno[*1,2,3-c,d*]pyrene, dibenz[*a,h*]anthracene and benzo[*g,h,i*]perylene.

0.1-unit increase in B[*a*]P DNA adducts per 10^8 nucleotides measured at birth was associated with two-times greater likelihood of developmental delay in motor dimension at the age of two years *(250)*. However, following the shut-down of the Tongliang power plant in 2004, lower (0.20 per 10^8 nucleotides) B[*a*]P adduct levels in cord blood were observed in a new cohort of children *(251)*. Subsequently, in 2005, cord blood B[*a*]P adducts were not associated with a reduction in developmental status at two years of age *(251)*.

Human carcinogenic risk

Early biological effects of PAH exposures have been examined in children in a small number of studies. A group of rural Indian children had significantly higher blood PAH concentrations (125.55 ± 26.99 ppb) than those from an urban region (23.96 ± 13.46 ppb), consistent with higher home exposure to the burning of wood, coal, cow dung and kerosene *(252)*. The extent of lipid peroxidation in whole blood was positively, albeit weakly, correlated with their total PAH and carcinogenic PAH levels in whole blood *(252)*. Among school-age children in Bangkok, the major source of exposure was road traffic.

When a group of Bangkok children were compared to a group of rural children, those from Bangkok had 3.5-fold higher exposure to B[*a*]P-equivalent compounds (mean 1.50 ± 0.12 vs 0.43 ± 0.05 ng/m^3). The Bangkok children's corresponding urinary 1-hydroxypyrene levels were significantly higher than those of the rural children. Furthermore, the levels of lymphocyte PAH-DNA adducts in the Bangkok children were 5-fold higher than those for the rural schoolchildren (0.45 ± 0.03 vs 0.09 ± 0.00 adducts/10^8 nucleotides). The frequency of DNA strand breaks was significantly higher, while the DNA repair capacity was significantly impaired in the Bangkok children compared to the rural children *(253)*.

In Prague, the mean personal exposure to 1.6 ng/m^3 of B[*a*]P during winter was associated with an elevated level of PAH-DNA adducts in a group of policeman *(254)*. Compared to the non-smoking controls (mean B[*a*]P = 0.8 ng/m^3), the frequency of chromosomal translocations for the policemen was significantly higher, based on fluorescence in situ hybridization (FISH) *(255)*. Within each individual subject, the level of "B[*a*]P-like" DNA adducts was a significant predictor of genomic frequency of translocations as detected in terms of FISH, percentage of aberrant cells and aberrations per cell *(255)*. In other groups of city policemen in Prague, DNA adducts were also positively correlated with genomic frequency of translocations *(254,256)*. Corresponding personal exposure to B[*a*]P was 1.6 ng/m^3 vs 0.4 ng/m^3 (in controls) *(254,256)*. Personal B[*a*]P exposure > 1.0 ng/m^3 also increased the micronuclei measured by automated image analysis *(257)* as well as DNA fragmentation in sperm *(268)* in the group of city policemen. All these results from biomonitoring studies indicate that exposure to B[*a*]P concentrations > 1.0 ng/m^3 induce DNA damage.

Carcinogenic effects of exposure to PAHs

In 2005, an IARC working group evaluated a number of occupational exposures to PAH-containing complex mixtures for their potential to induce cancer in humans. Occupational exposures during chimney sweeping, aluminium production, coal gasification, coke and steel production, coal-tar distillation, and paving and roofing with coal-tar pitch have been classified as carcinogenic to humans (Group 1). Occupational exposures to PAH-containing complex mixtures have been strongly associated with lung cancer and some of these exposures have a highly suggestive association with bladder and urinary tract tumours *(259)*. In addition, B[*a*]P was upgraded to a human carcinogen, based on sufficient evidence of carcinogenic activity in animals and strong evidence that the mechanisms of carcinogenicity in animals operate in humans *(259)*. The working group also updated a list of probable carcinogens to humans (Group 2A) and possible carcinogens to humans (Group 2B), as shown in Table 6.11. Cigarette smoke contains PAHs and cigarette smoking has also been classified as carcinogenic to humans *(260)*.

Table 6.11. IARC Classification of agents and occupations

Group 1: carcinogenic to humans	Group 2A: probably carcinogenic to humans	Group 2B: possibly carcinogenic to humans
Occupational exposure during coal gasification	Occupational exposure during carbon electrode manufacture	Benz[*j*]aceanthrylene
Occupational exposure during coke production	Creosote	Benz[*a*]anthracene
Occupational exposure during coal-tar distillation	Cyclopenta[*cd*]pyrene	Benzo[*b*]fluoranthene
Occupational exposure during chimney sweeping	Dibenz[*a*,*h*]anthracene	Benzo[*j*]fluoranthene
Occupational exposure during paving and roofing with coal-tar pitch	Dibenzo[*a*,*l*]pyrene	Benzo[*k*]fluoranthene
Occupational exposure during aluminium production		Benzo[*c*]phenanthrene
B[*a*]P		Chrysene
Diesel exhaust		Dibenzo[*a*,*i*]pyrene
ETS		Dibenzo[*a*,*h*]pyrene; indeno[1,2,3-*c*,*d*]pyrene; 5-methylchrysene

Mutagenic and carcinogenic risk of PAH-DNA adducts in adults

PAH-DNA adduct formation represents one of the key first steps in carcinogenesis *(261)*. PAH/aromatic DNA adducts have been associated with increased lung cancer risk in some molecular epidemiological studies. In a nested case-control study, healthy volunteers with detectable adduct levels in their leukocytes at the outset of the study were at two-fold greater risk of lung cancer than those with non-detectable levels *(262)*. In particular, never-smokers with a detectable adduct level were at four-fold higher lung cancer risk than those with a non-detectable level *(262)*. When the exposure was dichotomized at the median (0.6 DNA adducts per 10^8 nucleotides), the non-smokers with greater than median adduct levels were at seven-fold greater risk of lung cancer than those with non-detectable adducts *(262)*. In a small cross-sectional case-control study, those within the highest quartile of leukocyte PAH-DNA adduct levels (> 1.52 PAH-DNA adducts per 10^8 nucleotides) were at three-fold greater risk of colorectal adenoma than the lowest quartile of the adducts (≤ 0.71 adducts per 10^8 nucleotides) *(263)*.

In population-based case-control studies, the detectable level of PAH-DNA adducts has been associated with a 29–35% elevation in breast cancer risk *(261)*. Several genetic variants have been examined for their role in cancer development. A variant allele (GA or AA) in the FAS1377 gene was associated with a 36% increase in breast cancer risk among those with detectable PAH-DNA adduct levels *(264)*. However, variants of other genes, including GSTA1, GSTM1, GSTP1 and GSTT1, did not modify the risk *(265)*, while any dose–response relationship was consistently absent in several molecular epidemiological investigations *(261,266,267)*. In a large population-based cohort, detectable PAH-DNA adducts, measured at the time of the patient's breast cancer diagnosis, were not associated with subsequent all-cause or breast-cancer-specific mortality *(268)*. In a prospective follow-up study of prostate cancer, the risk of biochemical recurrence one year after surgical removal of the tumour was twofold greater in those with higher than the median level of prostate-specific adducts *(269)*.

Quantitative estimates of carcinogenic effects at occupational exposure range

In a combined meta-analysis of the aluminium production, coal gasification, coke production, iron and steel, coal tar, carbon black and carbon electrode production industries, cumulative B[*a*]P exposure concentrations over the working years ranged from 0.75 to 805 μg/m^3-years, equivalent to a concentration range of 0.04–40 μg/m^3 *(270)*. The mean relative risk of lung cancer increased by between 20% and 168% per 100 μg/m^3-years *(270,271)*. The mean risk remained robust when study design, smoking status and exposure measurement were accounted for *(270)*. While risk sizes were consistent within each occupation, large variability in lung cancer risk was observed across the occupations. Such heterogeneity in relative risk was attributed to variability in occupation-related exposure range.

Another meta-analysis estimated the industry-specific relative risk of respiratory and urinary tract cancers *(272)*. Risk of lung cancer was significantly elevated for all examined industries *(272)*. In particular, within the aluminium smelting industry, 100 μg/m^3-years exposure to B[*a*]P (equivalent to 3.3 μg/m^3 for 30 years) was associated with a 2.68-fold greater likelihood of developing lung cancer *(271)*. While a significant departure from linearity was observed in this analysis, indicating that the unit risk might be smaller at the highest exposure range, this pooled estimate sufficiently accounted for confounding by smoking *(271)*.

The risk of bladder cancer was significantly elevated only for those involved in aluminium production.

Conclusions

- Sources of airborne PAHs indoors are infiltration by PAHs in outdoor air and indoor emissions from smoking, domestic cooking and heating with fuel-burning stoves, open fireplaces, and incense and candle burning.
- In the absence of indoor sources, indoor concentrations of PAHs are lower than those outdoors.
- When indoor sources are present, indoor concentrations are likely to exceed those outdoors.
- In industrialized countries, ETS appears to have the greatest impact on indoor PAH concentrations, while in developing countries it is cooking and heating with solid and biomass fuels.
- In industrialized countries, inhalation is a minor route of exposure for non-smokers compared with dietary ingestion.
- In developing countries, inhalation is at least as important a route of exposure as dietary exposure.
- A sufficient body of evidence supports the causal role of PAH/aromatic DNA-adducts in lung cancer occurrence among non-smokers.
- B[*a*]P at levels above 1.0 ng/m^3 predicted greater genomic frequency of translocations, micronuclei and DNA fragmentation.
- Prenatal exposure to PAHs is associated with an increase in the likelihood of low birth weight.
- B[*a*]P and many other PAHs induce cancer by a mutagenic mechanism that involves metabolic activation to reactive diol-epoxides that covalently bind to DNA. These PAH-DNA adducts have been detected in tissues from experimental animals exposed to PAHs, and B[a]P-DNA adducts have been found in human lung tissues.
- PAH-DNA adducts are converted into mutations after cell replication, and mutations in critical tumour oncogenes and tumour suppressor genes have been identified in lung tumours from both experimental animals and humans exposed to PAHs or PAH-containing mixtures.

- Sufficient evidence exists of a link between the prenatal exposure to mixtures of carcinogenic PAHs and intrauterine growth restriction in humans.
- There is a robust body of evidence supporting a strong association between occupational exposure to PAH-containing mixtures and lung cancer in humans.

Health risk evaluation

Critical health outcomes

Biomarkers of exposure and effects

A growing body of evidence suggests that exposure to B[*a*]P at levels over 1.0 ng/m^3 induces DNA damage. Personal exposure to B[*a*]P over 1.0 ng/m^3 predicted greater genomic frequency of translocations, micronuclei and DNA fragmentation in sperm. In children in various developing countries, a number of markers for cytotoxic and oxidative stress have been positively correlated with either monitored personal PAH concentration or carcinogenic PAH levels in whole blood. Further, elevated exposure to B[*a*]P has been associated with higher levels of PAH-DNA adducts, urinary 1-hydroxypyrene, DNA strand breaks and impaired DNA repair capacity.

Intrauterine growth restriction

Intrauterine growth restriction has been defined in terms of low birth weight (< 2500 g), low birth weight at full-term (≥ 37 weeks) or SGA (< 10th percentile of population mean weight at a given gestational age and gender). A strong body of data demonstrates a significant role of prenatal exposure to particle-bound PAHs in reduced or low birth weight in Europe and the United States *(236)*. The direction and size of birth weight reduction are consistent overall. In addition, prenatal exposure to several PAHs induced severe fetotoxic effects in several animal species. Thus, it is concluded that sufficient evidence exists of a relationship between prenatal exposure to mixtures of carcinogenic PAHs and intrauterine growth restriction in humans.

Lung cancer

Occupational exposure to complex mixtures containing PAHs has been strongly associated with lung cancer. Studies on experimental systems have shown many PAHs to be genotoxic and carcinogenic. A detectable level of leukocyte PAH/bulky DNA adducts in non-smokers was correlated with an increased risk of lung cancer compared to those with a non-detectable level. When coded as a continuous variable, each unit increase in DNA adducts led to a 25 % increase in the risk of lung cancer, without a threshold. In occupational settings, with B[*a*]P exposure ranging between 0.04 and 40 μg/m^3, the risk of lung cancer increased by 20–168% per 100 μg/m^3 B[*a*]P-years. As a result, sufficient evidence of a causal relationship is considered to exist between exposure to mixtures of airborne

PAHs containing B[*a*]P and lung cancer. There is a sufficient body of evidence to support the critical role of PAH/bulky DNA adducts, mutations in tumour oncogenes and tumour suppressor genes in the development of lung cancer following exposure to PAHs.

Bladder cancer

Risk of bladder cancer has often been examined along with that of lung cancer in investigations of occupational exposures to PAHs. The risks were significantly elevated for some industries involving exposure to complex mixtures containing PAHs, namely aluminium production, paving and roofing, and chimney sweeping. Experimentally, PAHs have not been shown to induce bladder cancer. It is concluded that insufficient evidence exists of a relationship between exposure to mixtures of airborne PAHs containing B[*a*]P and bladder cancer.

Breast cancer

Risk of breast cancer has been examined mostly in terms of detectable levels of PAH-DNA adducts. A modest (29–35%) elevation in the likelihood of breast cancer diagnosis has been observed for those with detectable levels of PAH-DNA adducts compared to non-detectable levels, without an apparent dose–response relationship. However, when the follow-up was continued to the point of death, the detectable PAH-DNA adducts did not increase the risk of all-cause or breast cancer mortality. It is concluded that insufficient evidence exists for a relationship between exposure to mixtures of airborne PAHs containing B[*a*]P and breast cancer.

Fatal ischaemic heart disease

In experimental animals, PAHs including B[*a*]P, dibenz[*a,h*]anthracene, dibenz[*a,c*]anthracene and 7,12-dimethylbenz[*a*]anthracene have accelerated atherosclerosis plaque formation *(198,199)*. Following several inconclusive studies, a multinational cohort of male asphalt workers suggested that risk of ischemic heart disease (IHD) was associated with B[*a*]P exposure in a dose–responsive manner. However, the authors could still not rule out the possibility of confounding by exposure to fine particulates in the occupational setting *(248)*. It is concluded that limited evidence exists for a relationship between exposure to mixtures of airborne PAHs containing B[*a*]P and IHD. If these findings are corroborated, the IHD mortality from PAH exposure would be higher than that for lung cancer.

Health relevance of indoor exposure

Since there is sufficient evidence that some PAHs, including B[*a*]P, are genotoxic carcinogens, no threshold can be determined and all indoor exposures are considered relevant to health.

Indoor airborne levels of PAHs are influenced not only by infiltration of outdoor PAHs but also by lifestyle-related indoor emissions. In particular, children and women in developing countries are exposed to multiple and season-dependent sources of PAHs, including domestic burning of wood, coal, cow dung and kerosene, as well as industrial coal-burning and road traffic. Indoor B[*a*]P levels in homes that use biomass and coal for heating and cooking range from 33 to 186 ng/m^3 (range of geometric means) compared to B[*a*]P levels generally less than 1 ng/m^3 in non-smoking homes in developed countries (typically based on a 24-hour mean). The indoor B[*a*]P concentrations in developing countries increase the inhalation doses (105–2523 ng/day; range of geometric means). Hence, in these situations, the inhalation of particle-bound PAHs is at least as important a route of exposure as dietary exposure.

Conclusions of other reviews

IARC *(273)* concluded, based on occupational studies, that there is sufficient evidence that coal gasification, soot (as found in occupational exposure of chimney sweeps), aluminium production, coal tar pitch (as encountered in paving and roofing), iron and steel founding and coke production cause human lung cancer *(259)*. There is sufficient evidence that aluminium production causes bladder cancer in humans.

There is limited evidence in humans for a causal association of soot and coal tar pitch with bladder cancer *(259)*. Indoor emissions from household combustion of coal are carcinogenic to humans (Group 1), inducing lung cancer. Indoor emissions from household combustion of biomass fuel (mainly wood) are probably carcinogenic to humans (Group 2A), inducing lung cancer. Emissions from high-temperature frying are probably carcinogenic to humans (Group 2A) *(259)*.

B[*a*]P was reclassified by IARC *(260)* as a human carcinogen (Group 1) based on sufficient evidence of carcinogenic activity in animals and strong evidence that the mechanisms of carcinogenicity in animals operate in humans *(259)*. Cigarette smoke contains PAHs and ETS has also been classified as carcinogenic to humans (Group 1) *(260)*.

WHO concluded in 2000 *(2)* that occupational epidemiology data should serve as the basis for the risk estimate. Based on epidemiological data from studies in coke-oven workers, a unit risk for B[*a*]P as an indicator in ambient air constituents was estimated to be 8.7×10^{-5} per ng/m^3, which is the same as that established by WHO in 1987 *(23)*.

Guidelines

Some PAHs are potent carcinogens and, in air, are typically attached to particles. The primary exposure to carcinogenic PAHs found in air occurs via inhalation of particles. PAHs occur in indoor air as complex mixtures, the composition of

which may vary from site to site. Experimental data on metabolism, gene expression and DNA adducts suggest that interactions between PAHs in mixtures may be complex and highly unpredictable for various PAH compositions (inhibitory, additive, synergistic).

In view of the difficulties in developing guidelines for PAH mixtures, B[*a*]P was considered to represent the best single indicator compound. Its toxicology is best known, most single PAH concentration data in ambient and indoor air are for B[*a*]P, and B[*a*]P has widely been used as an indicator compound for exposure in epidemiological studies.

The health evaluation data suggest that lung cancer is the most serious health risk from exposure to PAHs in indoor air. B[*a*]P is one of the most potent carcinogens among the known PAHs.

In its evaluation of PAHs as ambient air pollutants in 2000, WHO *(2)* expressed a unit cancer risk as a function of the concentration of B[*a*]P taken as a marker of the PAH mixture. Use of the same unit risk factor for indoor air implies that B[*a*]P represents the same proportion of carcinogenic activity of the PAH mixture as in the occupational exposure used to derive the unit risk. This assumption will not always hold, but the associated uncertainties in risk estimates are unlikely to be large.

Reducing exposure to B[*a*]P may also decrease the risk of other adverse health effects associated with PAHs.

Based on epidemiological data from studies on coke-oven workers, a unit risk for lung cancer for PAH mixtures is estimated to be 8.7×10^{-5} per ng/m^3 of B[*a*]P. This is the guideline for PAH in indoor air. The corresponding concentrations for lifetime exposure to B[*a*]P producing excess lifetime cancer risks of 1/10 000, 1/100 000 and 1/1 000 000 are approximately 1.2, 0.12 and 0.012 ng/m^3, respectively.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome for guideline definition

Lung cancer is the most serious health risk from exposure to PAHs in indoor air. B[*a*]P is one of the most potent carcinogens among the known PAHs.

Source of exposure–effect evidence

There is sufficient evidence that some PAHs, including B[*a*]P, are genotoxic carcinogens. Based on epidemiological data from studies in coke-oven workers, a unit risk for B[*a*]P as an indicator of PAH in ambient air was estimated to be 8.7×10^{-5} per ng/m^3 *(2,23)*.

Supporting evidence

Studies on early biological effects of PAH exposure based on biomarkers in general populations of children and adults *(252–257)*, on carcinogenic effects in the occupational setting *(259)* and on mutagenic and carcinogenic risk of PAH-DNA adducts *(261–269)*.

Results of other reviews

IARC: B[*a*]P and PAH-containing indoor emissions from household combustion of coal have been classified in Group 1 (human carcinogens) *(259,260)*.

Guidelines

- No threshold can be determined and all indoor exposures are considered relevant to health.
- Unit risk for lung cancer for PAH mixtures is estimated to be 8.7×10^{-5} per ng/m^3 of B[*a*]P.
- The corresponding concentrations for lifetime exposure to B[*a*]P producing excess lifetime cancer risks of 1/10 000, 1/100 000 and 1/1 000 000 are approximately 1.2, 0.12 and 0.012 ng/m^3, respectively.

Comments

B[*a*]P is taken as a marker of the PAH mixture. Use of the B[*a*]P unit risk factor assumes that B[*a*]P represents the same proportion of carcinogenic activity of the PAH mixture in all indoor environments as in the occupational setting. This assumption will not always hold, but the associated uncertainties in risk estimates are unlikely to be large.

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7. Radon

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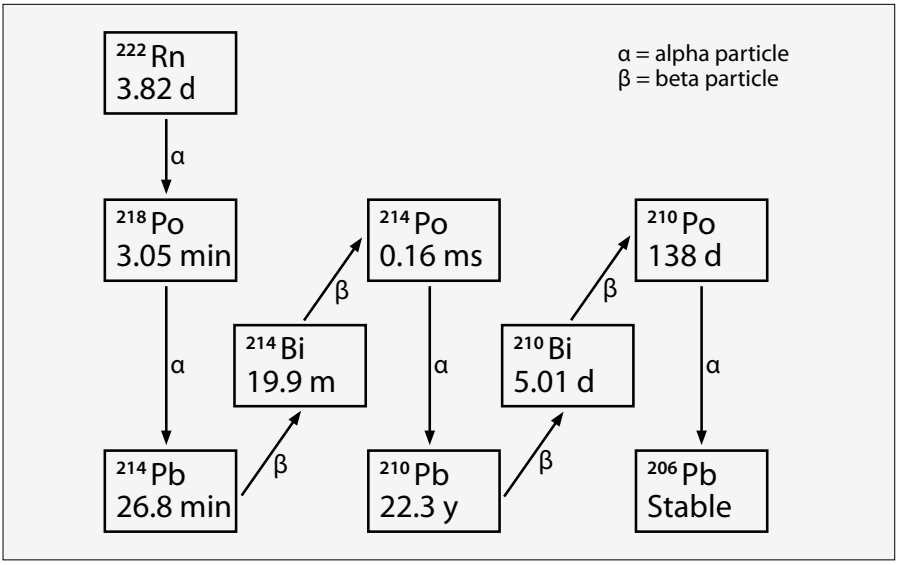
General description

Radon gas is an important source of ionizing radiation of natural origin and a major contributor to the ionizing radiation dose received by the general population. It comes mainly from exposure to radon and its airborne decay products in the homes of the general population *(1,2)*. Radon, which has a number of isotopes, is a naturally occurring colourless and odourless radioactive noble gas. The most stable of the isotopes is radon-222 (^{222}Rn) (half-life 3.826 days), which is universally and henceforth here referred to simply as "radon" or "radon gas". It is a member of the uranium-238 (^{238}Ur) decay series (half-life 4.5 × 10^9 years) and its immediate parent is radium-226 (^{226}Ra) (half-life 1620 years). Radon formed by the decay of radium in soil and rocks and entering the indoor air spaces of buildings or other enclosed locations (such as mines, tunnels or other underground workplaces) may reach concentrations of concern for health. Fig. 7.1 is a simplified decay scheme of radon-222 showing its principal short-lived progeny of radiological importance.

Fig. 7.1. Simplified decay scheme for radon, with isotpes and half-lives



Conversion factors and units

The SI unit for the activity of a radioactive substance is the becquerel (Bq), which is one radioactive decay per second. In indoor air, the degree of radioactive equilibrium between its airborne short-lived progeny and radon gas depends on several factors, principally on the aerosol concentration and its size distribution, the surface-to-volume ratio of the room and the air exchange rate. The degree of equilibrium is usually expressed in terms of the equilibrium factor (F factor), whereby an F factor of 1 means full radioactive equilibrium between radon and its airborne short-lived progeny. The F factor is important for determining the dose to the lungs from radon progeny. Measurements in several countries have shown F factors in dwellings to generally lie between 0.2 and 0.8. The United Nations Scientific Committee on the Effects of Atomic Radiation (UNSCEAR) and the International Commission on Radiological Protection (ICRP) have adopted a typical worldwide F factor of 0.4 for indoor air *(1,3)*. The F factor in outdoor air is usually somewhat higher, in the range 0.6–0.8.

Owing to these considerations, there are several measures used to describe airborne radon decay products. A commonly used measure is the equilibrium equivalent radon concentration, which is the activity concentration of radon (given in Bq/m^3) in equilibrium with its short-lived decay products that would have the same potential alpha energy concentration as the actual non-equilibrium mixture present in the air being measured. The potential alpha energy concentration is the sum of the potential alpha energy per unit volume of the short-lived radon progeny in the decay chain down to ^{210}Pb (half-life 22.3 years); its SI unit is J/m^3.

The potential alpha energy exposure of workers was historically expressed in terms of the working level month (WLM). Here one working level (WL) is any combination of short-lived radon progeny that will result in the ultimate emission of 1.3×10^5 MeV of potential alpha energy. This is approximately the alpha energy released by the decay of radon progeny in equilibrium with 3.7 Bq of radon. The WLM exposure unit was introduced and is still used to specify occupational exposure to 1 WL for a working month of 170 hours.

Analytical methods

Most of the radiation dose and hence the risk from radon is due to its short-lived alpha-particle-emitting polonium decay products (polonium-218 and polonium-214). Radon gas itself contributes a much smaller dose than these decay products. As an equilibrium factor of 0.4 is taken as being representative of indoor air in most homes, a measurement of radon gas is considered in general to be a good surrogate for estimating the concentrations of these decay products. Radon gas measurement is also technically much simpler and cheaper than measuring the decay products. Owing to both the effects of building usage practices (i.e. ventilation and heating) and meteorological variables, indoor

radon concentrations may exhibit quite large diurnal and seasonal variations. In the case of meteorological variables, their effects on radon exhalation from the ground and entry to dwellings is quite complex, with changes in atmospheric pressure, wind speed and precipitation being most important in this regard. As a consequence of these weather effects, in addition to diurnal and seasonal variations, indoor radon concentrations show substantial year-to-year variability.

To make a reliable estimate of the radon risk, it is thus necessary to make long-term (three months to a year) measurements of radon *(4)*. For measurements of a few months, a seasonal adjustment factor, if available, may be applied to obtain an estimate of the annual average value. Measurements made during the course of a single year also need correction for the aforementioned year-to-year variation *(5)*. From a health assessment perspective, short-term measurements of radon (duration of some days) are of limited use but may be of use in radon screening surveys to identify locations with a potential for high radon concentrations or when remediating a dwelling with a radon problem.

Owing to their low unit cost and reliability, the most popular devices used for making long-term radon measurements in European countries are small, passive devices using alpha-particle-sensitive material. These solid state nuclear track materials record the damage in the form of sub-microscopic latent tracks caused by alpha particles from radon and its decay products striking their surface. The latent tracks caused by the alpha particles striking the detector material are enlarged and made visible for optical microscopy by chemical or electrochemical etching *(6)*. These radon detectors are very simple and rugged in construction. They consist of a small piece of the alpha track material mounted inside a pill-box-sized chamber into which radon gas may diffuse. These detectors are passive as they do not require electrical power. The most commonly used alpha-particle-sensitive materials used in these detectors are polyallyl diglycol carbonate (CR-39), cellulose nitrate (LR-115) and polycarbonate (Makrofol). After exposure to radon and subsequent processing, the measured alpha track density is directly proportional to the integrated radon exposure in Bq/hour per m^3. The conversion from track density to the mean radon concentration over the exposure period is achieved by controlled exposure of the detector to a calibrated concentration of radon in a sealed exposure chamber. Comparisons between laboratories in Europe measuring radon take place regularly at the Radiation Division of the Health Protection Agency in the United Kingdom (formerly the National Radiological Protection Board), having originally been organized jointly with the European Commission *(7)*.

In addition to the alpha track passive detectors described above, passive charged electret radon detectors are also available, as well as a range of electronic continuous monitors of both radon gas and its decay products *(4,8,9)*.

These techniques are useful in determining contemporary indoor radon levels. In residential radon epidemiological studies, contemporary radon levels in

the present and in previous dwellings of a person are generally used as surrogates for the unknown radon levels in these dwellings in the past. Indoor radon levels can, however, be quite variable on diurnal, seasonal and annual timescales and can also be affected by changes in indoor living habits over time. Because of this, using contemporary indoor radon measurements as surrogates for indoor radon levels in past decades poses challenges to the assessment of long-term past exposure to radon.

Retrospective techniques based on the measurement of the build-up in a dwelling over many years of long-lived radon progeny such as polonium-210 in glass (the surface trap technique) or in porous media (the volume trap technique) can give some insight into the indoor radon concentration in a dwelling in past decades *(10,11)*. Direct in vivo measurements of lead-210 in the human skeleton have also been used to assess exposures in the past *(12)*.

Sources, occurrence in air and exposure

Indoor air

All rocks contain some uranium, typically at concentrations of 1–3 ppm. The uranium content of a soil will be about the same as the uranium content of the rock from which the soil was derived. As radium-226, the immediate parent of radon, is a decay product of uranium, the higher the uranium content of the soil the greater the radium concentration and the higher the chance that houses built on such soil will have high levels of indoor radon. The main source of indoor radon is the radon produced by the decay of radium in the soil subjacent to a house. Soil gas containing radon enters a house through cracks and fractures in the foundations by pressure-driven flow, as the air in a house is generally warmer and therefore at a lower pressure than the subjacent soil gas *(13)*. Radon concentrations in soil air/gas typically range from less than 10 000 Bq/m^3 up to 100 000 Bq/m^3. Most houses draw less than 1% of their indoor air from the soil; the remainder comes from outdoor air, which is generally quite low in radon. Houses with poorly sealed foundations, built on high-permeability ground and with several entry points for soil gas may draw more than 10% of their indoor air from the soil. Even if the soil air has only moderate levels of radon, levels inside such houses may be very high.

In comparison to soil gas, the radon exhaling from building materials in most cases does not significantly contribute to indoor radon levels. The uranium and radium content of building materials will be similar to the rock or clay from which they are made. While this is generally low, there are some building materials that may have high concentrations of radium. Examples of these are alum shale concrete and building materials made of volcanic tuff, by-product phosphogypsum, and some industrial waste materials *(14)*.

Water supplies can also contribute to indoor radon levels. River and surface reservoir water supplies usually contain very little radon but groundwater may

contain high concentrations, depending on the uranium/radium content of the aquifer formation. Public waterworks using groundwater and private domestic wells often have closed systems and short transit times that do not remove radon from the water or permit it to decay. This radon is out-gassed from the water to the indoor air when the water is used for washing, cooking and other purposes in a house. The areas most likely to have problems with radon in groundwater are those that have high levels of uranium in the underlying rocks. Radon concentrations can reach several thousand Bq/l in water from drilled wells in regions with granite rock or other uraniferous rocks and soils *(15)*. This contributes to indoor radon and to exposure via ingestion but the dose to the lung per unit exposure arising from inhalation is much higher than that owing to ingestion *(16)*. A very rough rule of thumb for estimating the contribution of radon in domestic water supplies is that house water with 10 000 Bq/m^3 radon contributes about 1 Bq/m^3 to the level of radon in the indoor air.

The range and distribution of indoor radon levels in many countries have been determined both by national surveys and in other investigations. Table 7.1 gives a summary of indoor radon surveys that have been carried out in a number of European countries *(17)*. It should be noted, however, that the survey design was not the same for each country. In some countries, dwellings were selected on the basis of population density. In this approach, more measurements are made in large centres of population than in sparsely populated rural areas. This enables estimates to be made of the collective exposure and health risk of the general population in a country. Such information is useful for developing national radon control strategies by the relevant authorities. Some national surveys were made on a geographical basis, where the strategy was to achieve the same density of dwelling sampling per unit area irrespective of the national population density distribution. Notwithstanding these differences, the data presented here give a reasonably accurate overview of average radon concentrations in contemporary European dwellings. It should also be noted that the maximum radon concentration values quoted in Table 7.1 are the maximum values found in national survey data. In many countries, much higher indoor radon concentrations have been found in targeted surveys carried out in areas where high radon levels were expected to be present on the basis of geological characteristics. The results of such surveys yield an erroneously high average radon concentration when extrapolated to the whole country. Table 7.2 gives a summary of indoor radon data for a number of large non-European countries *(1)*. It should be noted that representative national surveys of indoor radon have not yet taken place in countries with the largest populations, such as China and India.

The only other radon isotope that can occur indoors in significant amounts is radon-220 (half-life 55.6 seconds). Radon-220 is referred to as thoron and is a member of the thorium-232 (half-life 1.4×10^{10} years) decay series. Its immediate parent is radium-224 (half-life 4.6 days). It should be noted that there has

Table 7.1. Radon surveys in dwellings in some European countries

Country and population (millions)	No. of dwellings sampled	Period and approximate duration of measurement per dwelling
Austria (8.2)	16 000	1991–2002 3 months
Belgium (10.4)	10 447	1995–present 3 months
Croatia (4.5)	782	2003–2005 1 year
Czech Republic (10.2)	> 150 000	1984–present 1 year
Denmark (5.5)	3120	1995–1996 1 year
Finland (5.2)	3074	1990–1991 1 year
France (62.2)	12 261	1980–2003 3 months
Germany (82.4)	> 50 000	1978–2003 1 year
Greece (10.8)	1277	1994–1998 1 year
Ireland (4.2)	11 319	1992–1999 1 year
Italy (58.0)	5361	1989–1998 1 year
Luxembourg (0.49)	2619	1993–2002 3 months
Netherlands (16.6)	952	1995–1996 1 year
Norway (4.6)	37 400	1990–1999 2 months
Poland (38.5)	2886	1992–1994 3 months
Portugal (10.7)	3317	1988–1991 2.5 months
Slovenia (2.0)	892	1993–1995 3 months
Spain (40.5)	5600	1990–2005 3 months
Sweden (9.0)	1360	1991–1992 3 months
Switzerland (7.6)	55 000	1980–2005 3 months
United Kingdom (61.0)	450 000	1980–2005 3–12 months

Source: compiled mainly from National Summary Reports at http://radonmapping.jrc.ec.europa.eu/.

been an increasing interest in indoor thoron in recent years. Owing to its short half-life, thoron in soil gas beneath a building, in most situations, cannot survive long enough to enter a house and thereby contribute to the level of thoron in indoor air. Indoor thoron is due to the exhalation of thoron from thorium that may be present in the materials forming the internal surfaces of the building. Some building materials, such as volcanic tuff in Italy, have been found to have a high thoron exhalation rate. While in general indoor thoron levels are low, research in recent years has identified uncommon situations, such as cave dwellings, where the doses from airborne thoron decay products can be significant and can even exceed those from the radon decay products in the same location *(18)*. In this context, it should be noted that for the same exposure (i.e. concentration by time) the dose from thoron decay products is estimated to be about four times that of radon decay products *(1,19)*. From the perspective of radiation dose to lung tissue due to inhalation, the most important airborne thoron decay product is lead-210 (half-life 10.64 hours). While lead-210 itself is a beta particle emitter when it decays in the lung, it gives rise to the alpha-emitting decay products bismuth-212 (half-life 60.5 minutes, 36% alpha particle energy $E\alpha$ = 5.5–6.1 MeV) and polonium-212 (half-life 3×10^{-7} seconds, alpha particle energy $E\alpha$ = 8.68 MeV).

Mean Bq/m³	Geometric mean Bq/m³	Percentage > 200 Bq/m³	Maximum Bq/m³	Percentage > 400 Bq/m³
97	61	12	8325	4
69	76	2.4	4500	0.5
68	n/a	7.2	751	1.8
140	110	12–18	25 000	2–3
53	64	2.9	590	0.2
120	84	12.3	33 000	3.6
89	53	8.5	4964	2
49	37	1.6	> 10 000	0.45
55	44	3.1	1700	1.1
89	57	7.5	1924	1.5
70	52	4.1	1036	0.9
115	n/a	n/a	2776	3
30	25	0.3	382	<0.0001
89	n/a	9	50 000	3
49	n/a	2	3261	0.4
86	39	n/a	3558	n/a
87	n/a	7.7	1890	2
90	45	6	15 400	2
108	56	9–13	3904	3–4
77	n/a	17	29 705	7
20	n/a	0.5	17 000	0.1

Outdoor air

Land masses are the sources of outdoor radon while sea waters, having minimal radium concentrations, act as sinks. As a consequence, outdoor air radon levels are much lower (circa 0.1 Bq/m³) over oceans and seas than over a continental land mass such as mainland Europe *(20)*. Outdoor radon levels are determined mainly by the soil characteristics (uranium/radium content, porosity

Table 7.2. Radon concentrations in dwellings from surveys in some non-European countries

Country and population (millions)	Mean Bq/m³	Geometric mean Bq/m³	Geometric standard deviation Bq/m³	Maximum value Bq/m³
Argentina (39)	35	25	2	211
Australia (18)	11	8	2.1	420
Canada (30)	34	14	3.6	1720
China (1316)	44	34	—	596
India (945)	57	42	2.2	210
Japan (125)	16	13	1.8	310
Republic of Korea (49)	53	43	1.8	1350
United States (269)	46	25	3.1	—

Source: UNSCEAR *(1,21)*.

and the consequent radon exhalation rate), local topology and meteorological conditions. In some situations, such as atmospheric temperature inversions in valleys with high radon fluxes from the soil, short-term elevated outdoor radon levels have been observed. High outdoor radon levels are rare but could be of local health significance in areas such as former uranium mining districts, where elevated radon exhalation from tailing ponds combined with meteorological and topological conditions could give rise to high outdoor radon levels of seasonal duration. A direct proportionality in risk between indoor and outdoor radon exposures based simply on radon concentration and duration of exposure cannot, however, be assumed. This is because factors that influence the lung dose, such as the equilibrium factor between radon and its decay products (which are generally higher outdoors than indoors) and also aerosol characteristics, will be different indoors than outdoors.

National data on average outdoor radon levels are quite limited. It seems that they lie between 5 and 20 Bq/m^3 *(21)*. The ratio of the radon concentration in outdoor air to the mean indoor radon concentration in European countries (see Table 7.1) would appear to be in the range of about 7% (Czech Republic) to 20% (United Kingdom).

Routes of exposure

The most important route of exposure to radon and its decay products is inhalation. It is also possible to be exposed to radon by ingestion of water containing high radon concentrations but the dose and risk in this case are very small in comparison to those due to inhalation. In indoor air, radon produces a series of short-lived decay products that may attach to aerosol particles present in the air or deposit on room surfaces *(22)*. It is the inhalation and deposition in the airways of short-lived airborne radon decay products that give rise to irradiation by alpha particles of sensitive cells in lung tissue, such as the basal cells of the bronchial epithelium *(15)*. From considerations of their respective radioactive half-lives as well as their physical and chemical properties, the radiation dose delivered to the lung from inhaled radon decay products is dominated by the alpha particles emitted by the short-lived radon decay products polonium-218 (half-life 3.05 minutes, alpha particle energy E_α = 6.00 MeV) and polonium-214 (half-life 1.64×10^{-4} seconds, alpha particle energy E_α = 7.68 MeV). Because these alpha particles have respective ranges of only 48 μm and 71 μm in tissue, they deliver a high density of DNA damage to cells in these short distances.

Kinetics and metabolism

Absorption and doses

Dosimetry of inhalation of radon and its decay products is important in understanding the biological mechanisms and in estimating the effects of different factors that contribute to carcinogenesis *(21)*. Estimates of the absorbed dose per

unit of radon exposure to various organs and tissues can be derived from information on, for example, the unattached fraction, the activity/size distribution of the radon progeny aerosol, breathing rate, fractional deposition in the airways, mucus clearance rate, location of the target cells in the airways, and lung-to-blood absorption parameters. The doses to various lung tissues may be calculated using the ICRP human respiratory tract model *(23)* and other models. Dose estimates strongly depend on the choice of input parameters and other model assumptions, thus leading to some uncertainty in estimated absorbed doses *(24)*. The various dose calculation procedures and assumptions have been reviewed in detail in several reports *(1,21)*.

Kendall & Smith (*16*) estimated the doses to various organs and tissues from radon and its decay products, either by inhalation or ingestion or by deposition on the skin. With respect to inhalation, about 99% of the lung dose arises from radon progeny and not from the gas itself, as almost all of the gas that is inhaled is subsequently exhaled *(25)*. Radon decay products are largely deposited on the surface of the respiratory tract. Because of their relatively short half-lives, they decay mainly in the lung before being cleared either by absorption into the blood or by particle transport to the gastrointestinal tract. Thus, in the case of inhalation, the highest doses are to the lung and to the extra-thoracic airways (i.e. the nose, pharynx and larynx), while dose estimates to other organs and tissues were at least one order of magnitude lower. Outside the respiratory tract, the kidney is the organ most exposed to radon decay products. In general, the doses from radon gas are much lower than those from radon decay products. However, radon is more soluble in tissues with a higher fat content. As fat receives the highest dose of all tissues outside the lung, the doses to the red bone marrow and the female breast are somewhat higher. Kendall & Smith *(16)* also investigated the dose to the fetus. As the fat content of the fetus is low, its dose is assumed to be similar to that of the maternal muscle, which is estimated to be about 3–4 orders of magnitude smaller than the dose to the lung.

Kendall & Smith *(26)* also considered doses from radon and decay products when inhaled by one-year-old infants and ten-year-old children. They found that the general pattern of doses to organs is broadly similar to that of adults. The largest dose is received by the respiratory tract. Even though dose coefficients for children are generally larger than those for adults, the total annual doses are more similar because of the smaller intake of air by children. Radon decay products deposited on skin may be able to induce skin cancer. However, the location of the sensitive cells is not known with certainty and they may lie too deep to receive significant doses. On irradiation, it is likely that doses to children would be larger than those to adults.

Marsh et al. *(25)* recently provided a mathematical model to calculate the individual annual absorbed doses arising from radon and its decay products to regions of the lung, red bone marrow, liver and kidney among uranium miners of

the Czech, French and German cohort studies. Several exposure scenarios (wet/dry drilling, good/medium/poor ventilation, diesel engines, underground/surface, etc.) and levels of physical activity had been evaluated. For example, the scenario of underground work with wet drilling, medium ventilation and medium physical activity was estimated with the following annual absorbed doses in mGy/WLM: bronchial region 7.3, bronchiolar region 7.3, alveolar-interstitial region 0.45; red bone marrow 0.031, kidney 0.02 and liver 0.0065. As expected, the dose to the lung is the highest, as most of the short-lived radon progeny decay before they leave the lung. For the red bone marrow, the dose arising from the radon gas is greater than that from the radon progeny. Overall, the doses to red bone marrow, liver and kidney were appreciably lower than those to the lung.

Experimental animal studies

Animal studies have been conducted for several decades to evaluate the biological effects of inhaled radon and its decay products, mainly in rats but also in mice and beagle dogs. These studies systematically examined the pathogenic role of radon and its decay products, either alone or in various combinations with uranium ore dust, diesel-engine exhaust and cigarette smoke. In the late 1960s and early 1970s, it was proved that radon and its decay products, either alone or in combination, produce lung tumours *(21)*. Only a few laboratory animal studies investigated the risk of non-respiratory neoplasms, producing inconsistent results *(1,21,27,28)*.

A number of experimental animal studies examined the effects of exposure rate on induction of lung cancer, particularly at low cumulative exposures comparable to current underground mining exposures or to lifetime exposure in houses with high radon levels *(29–33)*. The results indicate that at low cumulative exposures, the risk of lung cancer increased with increasing exposure rate, while at high cumulative exposures (> 100 WLM), the reverse was observed (decreasing risk with increasing exposure rate). These data are consistent with that of underground miners showing an inverse exposure-rate effect at high cumulative exposures but a reduction of this effect at cumulative exposures lower than 50–100 WLM *(28,34–36)*. When biologically based models were applied to the various animal experimental data, the obtained set of significant model parameters appeared to compare reasonably well with that from similar models derived from studies on uranium miners *(37–40)*.

Molecular and cellular studies

Molecular and cellular radiobiology studies are important in understanding the mechanisms involved in carcinogenesis caused by ionizing radiation. In 1996, Jostes *(41)* provided an overview of the genetic, cytogenetic and carcinogenic effects of radon. He reported that radon and radon progeny cause cell transformation, changes in chromosome structure and gene mutations containing a wide

range of deletions, as well as base-pair changes. It is thus possible that even exposure to low radon concentrations such as in homes adds to the genetic load for cancer risk. Since then, a comprehensive review on cellular and molecular responses to various forms of radiation has been given by the Committee on the Biological Effects of Ionizing Radiation (BEIR VI) *(28)* and UNSCEAR *(1)*. The UNSCEAR report *(1)* includes specific annexes on DNA repair and mutagenesis, biological effects of low doses of ionizing radiation and the combined effects of exposure to radiation and other agents. An extensive update of this report, with specific focus on radon, is given in UNSCEAR's 2008 report *(21)*.

A number of in vitro studies of cells exposed to alpha-particle radiation demonstrated not only direct effects in irradiated cells but also non-targeted effects such as the bystander effect *(21)*. Bystander effects occur when irradiated cells emit signals that result in damage to nearby non-irradiated bystander cells. Brenner et al. *(42)* suggested that bystander effects can result in non-linear dose–response relations and inverse dose-rate effects, and thus make it difficult to extrapolate risks based on linear models of miner studies to the risk from residential radon *(43–45)*.

Chromosomal aberrations are among the most useful biomarkers of effects and doses from radon exposure *(1,21)*. Associations between chromosomal aberrations and cancer incidence have been observed in radon-exposed miners, while correlations between radon exposure and chromosomal aberrations have been found in radon-exposed miners and to some extent also in the general population through residential radon exposure *(21)*.

BEIR VI *(28)* and WHO *(4)* argued that it is possible that radon-related DNA damage can occur at any level of exposure to radon, since even a single alpha particle can cause major genetic damage to a cell. Therefore, it is unlikely that there is a threshold concentration below which radon does not have the potential to cause lung cancer.

Health effects

Identification of studies

Health effects of radon were identified by hand searching references in former reviews by UNSCEAR *(1,21)*, the National Research Council *(15,28)*, IARC *(46)* and WHO *(4)*. All these reports were published between 1988 and 2009. The detailed UNSCEAR report *Sources-to-effects assessment for radon in homes and workplaces* from 2008 *(21)* and the WHO radon handbook from 2009 *(4)* formed the major basis for the text. Next to that, electronic searches were made in PubMed in January 2009, with an update in December 2009 in order to identify newly published papers. The keywords were: "radon" and "cancer" or "health effects" or "mortality". Moreover, recent papers known to the experts were included. For the present review, next to the above-mentioned summary reports, approximately 50 publications on health effects in relation to radon exposure

were selected. About 70% of them concerned studies on miners with occupational underground radon exposure and 30% concerned indoor radon studies in the general population.

Effects on humans: lung cancer

Studies on miners

Since the 1960s, studies on underground miners have consistently demonstrated an increased risk of lung cancer caused by radon and its progeny *(15)*. Based on this evidence, IARC classified radon as a human carcinogen in 1988 *(46)*. Since then, several reviews on radon-related risk among miners have been published *(1,4,21,28)*.

In 1999, BEIR VI reported on the joint analysis of 11 miner cohort studies *(28)*. This collaborative study included a total of 60 000 miners, mainly miners of uranium but also of tin, fluorspar and iron from Asia, Australia, Europe and North America. Overall, a total of 2600 deaths from lung cancer had occurred. Lung cancer rates increased approximately linearly with increasing cumulative radon exposure in each study, but the magnitude of risk varied 10-fold between the individual studies. Based on the joint analysis of the 11 cohorts, the average excess relative risk (ERR) per WLM was estimated to be 0.44% (95% CI 0.20–1.00). The ERR/WLM decreased with increasing time since exposure and increasing attained age. In addition, the risk was modified by either exposure rate or duration of exposure. There was an inverse exposure rate effect, i.e. miners exposed at relatively low radon concentrations had a larger ERR/WLM than those exposed at higher radon concentrations. For some of the studies, information on smoking was available. When separate analyses for ever-smokers and never-smokers were performed, the ERR/WLM for never-smokers was higher than that for ever-smokers (1.02%; 95% CI 0.15–1.38 vs 0.48%; 95% CI 0.18–1.27), although this difference was not statistically significant. A potential limitation of the pooled cohort study concerns heterogeneity between the 11 cohorts with respect to differences in exposure quality, other occupational risk factors, lifestyle factors, etc.

Later, several more methodological papers were published based on existing miner cohorts *(47–51)*. To achieve some insight into the mechanisms involved in the genesis of cancer, various biologically based models have been applied to the data of the Czech, French, Colorado and Chinese miner cohort studies *(32,52–54)*. A detailed summary of these mechanistic studies is given the 2008 report from UNSCEAR *(21)*. The Czech *(55,56)*, French *(57–60)* and Newfoundland *(61)* cohort studies have been updated. Moreover, in comparison to data in BEIR VI (*28*), four new studies of radon-exposed miners have been established in Brazil *(62)*, the Czech Republic *(56)*, Germany *(34,36,63,64)* and Poland *(65)*.

The German Wismut cohort study *(34,36)* is similar in size to the pooled BEIR VI study *(28)*. It includes around 59 000 men who had been employed by the Wismut uranium mining company in eastern Germany. In the second mortal-

ity follow-up by the end of 2003, a total of 3016 deaths from lung cancer had occurred. Using a linear relative risk model, the average ERR/WLM was 0.19% (95% CI 0.16–0.22) *(36)*. The ERR/WLM was modified by time since exposure, attained age and exposure rate, but not by duration of exposure. When the exposure-age-concentration model of BEIR VI *(28)* was applied, there was a decrease in the ERR/WLM with time since exposure and attained age, as in the BEIR VI study, although the decrease with attained age was less pronounced. In both studies, a strong inverse exposure-rate effect above cumulative radon concentrations of more than 100 WLM was present. Information on smoking in the cohort was limited. A case-control study on incident lung cancer among German uranium miners, including detailed information on lifelong smoking habits *(66)*, found a somewhat larger ERR/WLM for never-smokers (0.20%; 95% CI 0.07–0.48) than for ex-smokers (0.10%; 95% CI 0.03–0.23) and current smokers (0.05%; 95% CI 0.001–0.14). The data pointed to a sub-multiplicative effect of the two factors, with no significant deviation from the multiplicative or the additive interaction model.

Tomasek et al. *(35)* investigated radon-associated risk, particularly at low exposure rates, based on a pooled analysis of the Czech and French cohorts, including a total of 10 100 uranium miners. These miners were characterized by low levels of exposure (average cumulative WLM < 60) over a long time (mean duration ~ 10 years) and by good quality of exposure (95% of the annual exposures are obtained by radon measurements). The overall ERR/WLM related to measured values was 2.7% (95% CI 1.7–4.3). It was strongly modified by time since exposure and age at exposure. No inverse exposure rate effect below 4 WL was observed. This result was consistent with estimates of the BEIR VI report *(28)* using the age-concentration model at an exposure rate below 0.5 WL.

Residential radon studies

There is substantial uncertainty in the extrapolation of the risk of lung cancer from the miners studies to the risk of lung cancer from radon exposure in the home *(28)*. For this reason, a series of epidemiological studies directly investigated the association between indoor radon and risk of lung cancer since the 1980s *(1,4,21,28)*. The first generation of these studies were ecological studies, in which average radon concentrations were correlated with average lung cancer rates at an aggregated geographical level. This type of study is known to be prone to bias because of several methodological problems *(1,21,67)*. Later, a number of case-control studies were carried out that gathered detailed information on smoking history and other risk factors for lung cancer and assessed the radon exposure retrospectively by measuring radon in the current and previously occupied homes of the study participants.

A detailed review of the results of these individual case-control studies is given in the 2008 report by UNSCEAR *(21)*. The majority of the studies showed

a positive association between radon exposure and risk of lung cancer; however, the estimated risk coefficients often did not reach statistical significance in the individual studies. Moreover, there was a substantial variation in the estimated radon-related risk as published in the individual studies. Several meta-analyses had been undertaken to summarize the findings *(68–70)*. Differences in the methodology used to analyse the different studies, such as adjustment for smoking and exposure quantification, however, limit the interpretation of these meta-analyses. For this reason, the original data of the individual studies were brought together and collaborative analyses were performed on the individual data of 13 European studies *(71,72),* 7 North American studies *(73,74)* and 2 Chinese studies *(75)*.

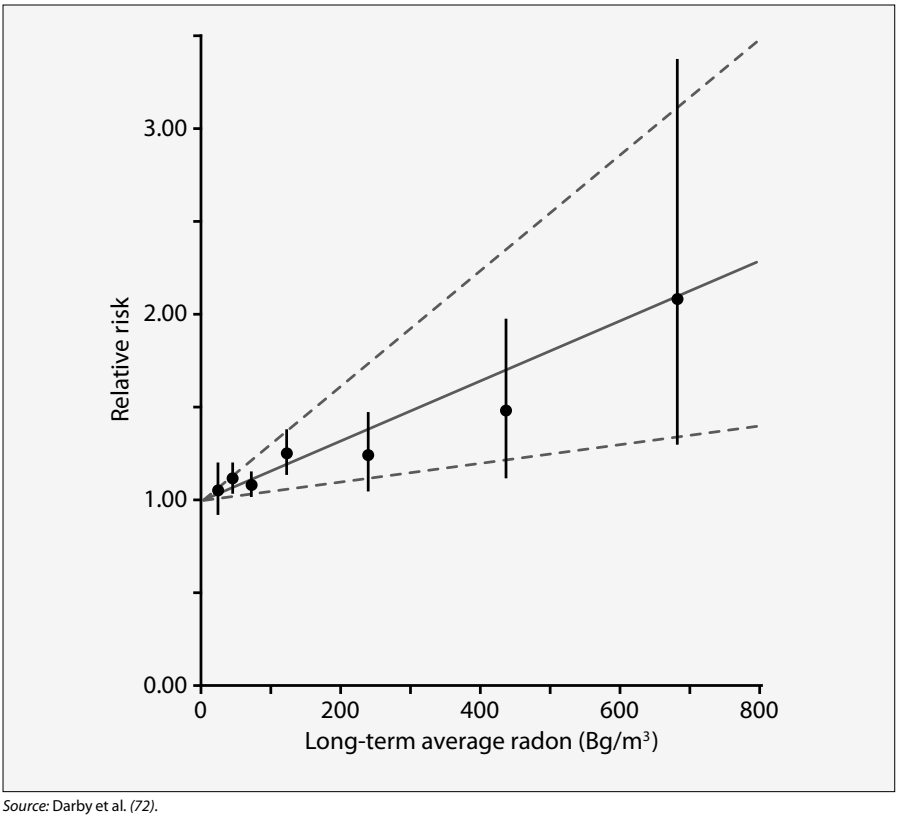
The largest of these pooled studies is the European pooling study published by Darby et al. *(71,72)*. It includes 7148 cases and 14 208 controls from 13 European indoor radon case-control studies on lung cancer, all with detailed information on smoking histories and radon measurements in homes that the individual had occupied for the past 15 years or more. The available radon measurements covered a mean of 23 years in the relevant radon exposure period 5–34 years prior to interview. Individual exposure to radon (called "measured" radon concentration) was calculated as the time-weighted average of the radon concentrations in all the homes occupied over the past 5–34 years, with missing radon values substituted by the mean concentration of the controls in that region. A statistical model was fitted in which the additional risk of lung cancer was proportional to measured radon concentration. In addition, radon exposure was subdivided into categories and the relative risk across categories of measured radon concentrations was plotted against the mean level in these categories. In both models, detailed stratification was performed for study, age, sex, region of residence and 25 smoking categories. Since no statistically significant heterogeneity in the radon-associated risk between the studies was present, the data were pooled.

In the pooled analysis, the excess relative risk of lung cancer per 100 Bq/m^3 "measured" radon concentration was 8% (95% CI 3–16). This proportionate increase did not differ significantly by study, age, sex or smoking history. The corresponding risk estimates for lifelong non-smokers, ex-smokers and current cigarette smokers were 11% (95% CI 3–28), 8% (95% CI 3–21) and 7% (95% CI –1 to –22), respectively. The exposure–response relationship appeared to be approximately linear, with no evidence for a threshold below which there was no risk. In particular, the results were incompatible with a threshold exposure below which there is no risk above 150 Bq/m^3. Even when the analysis was restricted to individuals with measured radon concentrations below 200 Bq/m^3, the exposure–response relationship remained statistically significant. The risk of lung cancer was 1.2-fold (95% CI 1.03–1.30) higher among individuals with measured radon concentrations of 100–199 Bq/m^3 than in those with concentrations < 100 Bq/m^3 and the increase was statistically significant.

Analysis based on the so-called "long-term average radon concentration", which takes into account the random year-to-year variability in measured radon concentration in the homes, led to a doubling of the excess relative risk of 16% (95% CI 5–31) per 100 Bq/m^3. Again, the risk did not differ significantly by study, age, sex or smoking status, and the exposure–response relationship was approximately linear (Fig. 7.2).

Darby et al. *(72)* also reported in detail on the combined effects of smoking and radon within the European pooled study. Table 7.3 gives information on the cumulative risk of death from lung cancer by the age of 75 years for lifelong non-smokers and continuing smokers of 15–24 cigarettes a day ("current smokers"). For these calculations, the estimated excess relative risk of 16% per 100 Bq/m^3 of long-term average radon concentration, which was independent of smoking status, was used. The relative risk for current smokers of 15–24 cigarettes per day compared to lifelong non-smokers was estimated as 25.8-fold. For lifelong non-smokers, it was estimated that living in a home with a long-term average radon concentration of 0, 400 or 800 Bq/m^3 was associated with a cumulative

Fig. 7.2. Relative risk of lung cancer vs long-term average residential radon concentration



Source: Darby et al. *(72)*.

Table 7.3. Cumulative risk of death from lung cancer by the age of 75 years for lifelong non-smokers and continuing smokers of 15–24 cigarettes per day at various radon concentrations [a]

Radon concentration (Bq/m³)	Risk of death per 1000 current smokers of 15–24 cigarettes per day	Risk of death per 1000 lifelong non-smokers
0	101	4.1
100	116	4.7
200	131	5.4
400	160	6.7
800	216	9.3

[a] After correction for uncertainties in the assessment of radon concentrations.

Source: Darby et al. *(72)*.

Note. Absolute risk of lung cancer for lifelong non-smokers taken from the prospective study of the American Cancer Society. Relative risk of lung cancer for continuing smokers of 15–24 cigarettes per day compared to lifelong non-smokers assumed to be 25.8. Relative risk of lung cancer assumed to increase by 0.16 per 100 Bq/m³.

risk of death from lung cancer of 41, 67 or 93 per 1000. For current smokers, the corresponding values would be 101, 160 or 216 per 1000, respectively. For those having stopped smoking, the radon-related risks are substantially lower than for those who continue to smoke, but they remain considerably higher than the risks for lifelong non-smokers.

Krewski and co-workers *(73,74)* reported on the results of the pooled analysis of seven indoor radon case-control studies in Canada and the United States, which included a total of 3662 cases and 4966 controls. Residential radon levels were measured for one year by alpha-track detectors. For each individual, the time-weighted average of the radon concentrations in the homes was calculated, with a focus on the period 5–30 years prior to the date of interview. Because no statistically significant heterogeneity of radon-related risk was found between the studies, a combined analysis was performed. Based on this joint analysis, the risk of lung cancer increased by 11% (95% CI 0–28) per 100 Bq/m³ increase in measured radon concentration. The trend was consistent with a linear exposure–response relationship. There was no apparent difference in the proportionate increase in risk by sex or smoking history, although there was some evidence of decreasing radon-associated lung cancer risk with age. Analyses restricted to individuals with presumed "more accurate dosimetry" resulted in increased risk estimates. For example, for individuals who lived in only one or two homes in the 5–30-year period and for which alpha-track measurements covered at least 20 years of this period, the proportionate increase in lung cancer risk was 18% (95% CI 2–43).

The Chinese pooled study published by Lubin et al. *(75)* included 1050 cases and 1996 controls from two studies in two areas, Gansu and Shenyang. As in the North American pooled study, the time-weighted average of the radon concentration in homes was calculated within the exposure period 5–30 years. No significant heterogeneity in the associated risk was present between the two stud-

ies. For the pooled data, the increase in risk per 100 Bq/m^3 increase in measured radon concentration was 13% (95% CI 1–36) and the results were consistent with a linear exposure–response relationship with no threshold. When analyses were restricted to individuals resident in only one home and with complete measurement coverage in the relevant period, the proportionate risk per 100 Bq/m^3 increased to 33% (95 CI 8–96).

In the *WHO handbook on indoor radon (4)*, a review and comparison of the risks are provided from all three pooled residential radon studies and the miner studies (Table 7.4). The radon-related risk estimates in the three pooled indoor radon studies were very similar. In each study, the exposure–response relationship appeared linear, without evidence of a threshold, and there was no statistically significant evidence that the radon-related risk varied by age, sex or smoking status. A weighted average of the three pooled risk estimates was provided, with weights proportional to their variances, resulting in a joint estimate of 10% proportionate increase in lung cancer risk per 100 Bq/m^3 measured radon concentration. WHO *(4)* estimated that, based on long-term average radon concentration instead of measured radon concentration, this 10% estimate could even increase to 20% per 100 Bq/m^3 if it is assumed that the effect of adjusting for year-to-year random variation in the three pooled studies combined is the same as in the European study.

In general, a direct comparison of the risks of lung cancer between residential and miner studies is difficult. This is due to the higher average radon exposures among miners and the time-dependent modifying factors, but primarily the inverse exposure rate effect. Thus, the summary estimates of the joint 11 miner studies and the German miner study are somewhat lower, with 5% and 3% per 100 Bq/m^3, respectively, than in the residential studies *(4)*. When analyses in the BEIR VI study were restricted to cumulative exposures below 50 WLM, which is comparable to living in a house with a radon concentration of around 400 Bq/m^3 for 30 years, the estimated risk coefficient increased to 14% per 100 Bq/m^3 *(76)* and even to 30% per 100 Bq/m^3 after additional restriction to miners with radon concentrations lower than 0.5 WL (i.e. < ~ 2000 Bq/m^3). No such risk analyses had been performed within the German study; assuming that the same restriction as in the BEIR VI study has the same effect, however, then the corresponding risk would be around 18% per 100 Bq/m^3. Based on the joint analysis of the Czech and French cohorts, which is characterized by low levels of cumulative exposures, an increase of about 29% per 100 Bq/m^3 would be expected in the exposure window 5–34 years.

Based on these comparisons, WHO *(4)* concluded that, in summary, the radon-related risk estimates for lung cancer from residential radon studies and studies of underground miners with relatively low cumulative exposures accumulated at low concentrations are in good agreement.

Table 7.4. Summary of risks of lung cancer from indoor radon based on international pooling studies that have combined individual data from a number of case-control studies and on studies of radon-exposed miners

	No. of studies included	No. of lung cancer cases	exposure window (years) [a]
Pooled residential studies			
European *(71,72)*	13	7148	5–35
North American *(73,74)*	7	3662	5–30
Chinese *(75)*	2	1050	5–30
Weighted average of above results			
Studies of radon-exposed miners [e,f]			
BEIR VI *(28,76)*	11	2787	≥ 5
		468	
		250	
German cohort study *(34)*	1	2388	≥ 5
Czech and French cohort studies *(35)*	2	574	≥ 5
			5–35

[a] Considering radon concentrations during the period starting 35 years before and ending 5 years before the date of diagnosis for cases of lung cancer, or a comparable date for controls.
[b] Adjusting for year-to-year random variability in indoor radon concentration.
[c] Estimate corresponding to higher coverage of measurements.
[d] Informal estimate, indicating the likely effect of removing the bias induced by random year-to-year variation in radon concentration.
[e] Risks per WLM have been converted to risks per 100 Bq/m^3 by assuming that 1 Bq/m^3 at equilibrium is equivalent to 0.00027 WL, that the "equilibrium factor" in dwellings is 0.40, that people spend 70% of their time at home, that there are 365.25 x 24/170 = 51.6

Effects on humans: diseases other than lung cancer

A number of studies focused on the relationship between radon and leukaemia in children and adults. Laurier et al. *(77)* reviewed 19 ecological studies, 8 residential case-control studies and 6 miner cohort studies published between 1997 and 2001. While the ecological studies suggested a positive correlation between residential radon exposure and leukaemia at a geographical level, the case-control studies and cohort studies did not. Overall, the authors concluded that the available data did not provide evidence of an association between radon and leukaemia *(77)*. Since then, a positive association between leukaemia incidence and exposure to radon has been reported in a case-cohort study among Czech uranium miners *(78)*, in a Danish case-control study on residential radon and childhood leukaemia *(79)* and in a French ecological study on childhood leukaemia *(80)*, while no evidence for an increased risk of leukaemia by exposure to radon was reported in two independent studies among German uranium miners *(81,82)*.

Overall, individual miner cohort studies have provided little evidence for an increased risk of cancers due to radon other than lung cancer *(28,58,83,84)*. However, most of these studies were limited owing to small numbers of cases.

Percentage ERR/100 Bg/m³ (95% CI) observed radon	Percentage ERR/100 Bg/m³ (95% CI) corrected for exposure uncertainties
8 (3–16)	16 (5–31) [b]
11 (0–28)	18 (2–43) [c]
13 (1–36)	33 (8–96) [c]
10	20 [d]
All miners	5 (2–12)
Miners < 50 WLM only	14
Miners < 0.5 WL only	19
Miners < 50 WLM and < 0.5 WL	30
All miners	3
Miners at low exposures and low exposure rates	18 [g]
Measured exposures	32 (14–34)
	29 (16–40)

"working months" in one year, and that the ratio of the dose to lung cells for exposures in homes to that for similar exposures in mines (sometimes referred to as the K-factor) is unity.

[f] Only one study *(48)* specifically addressed the effect of measurement error in the estimates of radon-related lung cancer risk in miners. This concluded that for miners exposed at concentrations below 15 WL, measurement error was of little consequence.

[g] Informal estimate, obtained by multiplying the estimate for all miners in the German cohort by 6, i.e. the ratio of the estimates for all miners and for miners exposed to < 50 WLM and < 0.5 WL from the BEIR VI analysis.

The two largest and most informative studies are the pooled analysis of 11 miner cohorts *(85)* and the German Wismut cohort study *(82)*. In the pooled study, the observed mortality from extrapulmonary cancers combined (O) was close to that expected from national rates (E) (n = 1179; O/E = 1.01; 95% CI 0.95–1.07). The trend with cumulative exposure was statistically significant only in the first decade since start of employment.

Among individual sites examined, a statistically significant excess in mortality was found for leukaemia and cancers of the stomach and liver (in the period less than 10 years since starting work). For none of the examined cancer sites was mortality significantly related to cumulative radon exposure, except for pancreatic cancer, which might be a chance finding.

In common with the pooled analysis of 11 miner cohorts, no excess in the overall mortality from extrapulmonary cancers was observed in the German Wismut cohort when compared to the general population (n = 3340; O/E = 1.02, 95% CI 0.98–1.05) *(82)*, while statistically significant excesses in mortality for cancers of the stomach and liver were present. When the relationship with cumulative radon exposure was considered, a statistically significant relationship was found for all extrapulmonary cancers combined (ERR/WLM = 0.014%; 95% CI 0.006–0.023)

and cancers of the extra-thoracic airways and trachea (ERR/WLM = 0.062%; 95% CI 0.002–0.121) *(64)*. The majority of non-respiratory cancer sites investigated revealed positive exposure–response relationships, which were non-significant however. The authors concluded that the study provides some evidence for an increased radon-related risk of cancers of the extra-thoracic airways and some other non-respiratory cancer sites; this is in line with calculations of organ doses, though chance and confounding cannot be ruled out. Based on a large case-control study on laryngeal cancer among German uranium miners, Mohner et al. *(86)* reported no relationship with cumulative radon exposure.

Epidemiological studies on diseases other than cancer mainly focused on the relationship between radon exposure and cardiovascular disease among miners. None of these studies found any evidence that radon causes cardiovascular diseases *(64,87–91)*. A Norwegian study demonstrated an association between multiple sclerosis and indoor radon, but this study was prone to bias owing to the ecological study design *(92)*.

Overall, the currently available epidemiological evidence indicates that there is only suggestive evidence that radon causes a material risk for diseases other than lung cancer.

Health risk evaluation

Definition of health outcomes

Health effects of radon, most notably lung cancer, have been investigated for several decades. An increase in the risk of lung cancer with increasing exposure to radon was first consistently demonstrated in studies on underground miners *(15,28)*. Based on these results, radon was classified by IARC in 1988 as a Group 1 human pulmonary carcinogen (*46*). In addition, there is direct evidence from epidemiological indoor radon studies that radon in homes increases the risk of lung cancer in the general population *(4,21)*.

The pooled analysis of data from the European *(71,72),* North American *(73,74)* and Chinese *(75)* residential radon studies consistently demonstrated that the risk of lung cancer increases approximately linearly with increasing long-term radon exposure. There is no known threshold below which radon exposure presents no risk. The increase is statistically significant even below 200 Bq/m^3. Risk estimates from epidemiological studies of miners and residential case-control studies are remarkably coherent. There is limited, though inconsistent, evidence of other cancer risks due to radon.

When radon gas is inhaled, densely ionizing alpha particles emitted by deposited short-lived decay products of radon can interact with biological tissue in the lungs, leading to DNA damage. Molecular and cellular studies demonstrated that it is possible that radon-related DNA damage can occur at any level of exposure to radon, since even a single alpha particle can cause major genetic damage to a cell *(1,4,21)*.

Relevance for health of current indoor exposures in various regions of the world

Radon is a major contributor to the ionizing radiation dose received by the general population. Outdoor radon levels are usually very low, with average values in the range of 5–20 Bq/m^3. National indoor radon surveys show that the distribution of radon concentrations in dwellings is approximately log-normal, with average values ranging between 20 and 150 Bq/m^3 *(4,93)*. Published estimates of the proportion of lung cancers attributable to residential radon exposure range from 3% to 14%, depending on the average radon concentration in the country concerned and the calculation methods *(4)*. As most people are exposed to low or moderate radon concentrations, the majority of lung cancers related to radon are caused by these exposure levels rather than by higher concentrations. In many countries, radon is the second cause of lung cancer after smoking. Most of the radon-induced lung cancer cases occur among smokers and ex-smokers owing to a strong combined effect of smoking and radon exposure. Nevertheless, radon exposure is the primary cause of lung cancer among people who have never smoked.

In summary, there is sufficient evidence to conclude that radon causes lung cancer, even at concentrations typically found in indoor air. There is suggestive evidence of an association with other cancers, in particular leukaemia and cancers of the extra-thoracic airways.

Guidelines

Radon is classified by IARC *(46)* as a human carcinogen (Group I). There is direct evidence from residential epidemiological studies of the lung cancer risk from radon. The exposure–response relationship is best described as being linear, without a threshold. The ERR, based on long-term (30 years) average radon exposure is about 16% per increase of 100 Bq/m^3 *(71,72)* and on this relative scale does not vary appreciably between current smokers, ex-smokers and lifelong non-smokers. Therefore, as the absolute risk of lung cancer at any given radon concentration is much higher in current smokers than lifelong non-smokers, the absolute risk of lung cancer due to radon is appreciably higher for current and ex-smokers than for lifelong non-smokers. For ex-smokers, the absolute risks will be between those for lifelong non-smokers and current smokers.

The cumulative risk of death from radon-induced lung cancer was calculated for lifelong non-smokers and for current smokers (15–24 cigarettes per day) *(72)*. The derived excess lifetime risks (by the age of 75 years) are 0.6×10^{-5} per Bq/m^3 and 15×10^{-5} per Bq/m^3, respectively. Among ex-smokers, the risk is intermediate, depending on the time since smoking cessation. The radon concentration associated with an excess lifetime risk of 1 per 100 and 1 per 1000 are 67 Bq/m^3 and 6.7 Bq/m^3 for current smokers and 1670 Bq/m^3 and 167 Bq/m^3 for lifelong non-smokers, respectively.

As part of the management of the radon problem, the WHO International Radon Project has recommended that there should be a reference level as an essential tool in this process *(4)*.

> A national Reference Level does not specify a rigid boundary between safety and danger, but defines a level of risk from indoor radon that a country considers to be too high if it continues unchecked into the future. However, protective measures may also be appropriate below this level to ensure radon concentrations in homes are well below that level. In view of the latest scientific data, WHO proposes a Reference Level of 100 Bq/m^3 to minimize health hazards due to indoor radon exposure. However, if this level cannot be reached under the prevailing country-specific conditions, the chosen Reference Level should not exceed 300 Bq/m^3 which represents approximately 10 mSv per year according to recent calculations by the International Commission on Radiation Protection.

A guide for radon management should include, in addition to the setting of a reference level, building codes, measurement protocols and other relevant components of a national radon programme *(4)*.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome(s) for guideline definition

- Lung cancer (sufficient evidence of causality even at concentrations typically found in indoor air).
- Suggestive evidence of an association with other cancers, in particular leukaemia and cancers of the extra-thoracic airways.

Source of exposure–effect evidence

The pooled analysis of data from the European *(71,72)*, North American *(73,74)* and Chinese *(75)* residential radon studies consistently demonstrated that the risk of lung cancer increases approximately linearly with increasing long-term radon exposure. There is no known threshold below which radon exposure presents no risk. The increase is statistically significant even below 200 Bq/m^3.

Supporting evidence

Risk estimates from epidemiological studies of miners *(15,28)* are consistent with residential studies. Molecular and cellular studies demonstrated that it is possible that radon-related DNA damage can occur at any level of exposure, since even a single alpha particle can cause major genetic damage to a cell *(1,4,21)*.

Results of other reviews

- IARC: Group I (known human carcinogen with genotoxic action) *(46)*.
- WHO International Radon Project: Reference Level of 100 Bq/m^3 *(4)*.

Guidelines

- The excess lifetime risk of death from radon-induced lung cancer (by the age of 75 years) is estimated to be 0.6 × 10–5 per Bq/m^3 for lifelong non-smokers and 15 × 10–5 per Bq/m^3 for current smokers (15–24 cigarettes per day). Among ex-smokers, the risk is intermediate, depending on the time since smoking cessation.
- The radon concentration associated with an excess lifetime risk of 1 per 100 and 1 per 1000 are 67 Bq/m^3 and 6.7 Bq/m^3 for current smokers and 1670 Bq/m^3 and 167 Bq/m^3 for lifelong non-smokers, respectively.

Comments

WHO guidelines provide a comprehensive approach to the management of health risks related to radon *(4)*.

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8. Trichloroethylene

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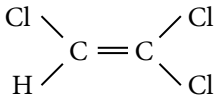
General description

Trichloroethylene (TCE) (CAS Registry Number, 79-01-6; $C_6H_3Cl_3$; molecular weight 131.40 g/mol) is a widely used industrial solvent. It is a volatile, colourless liquid with a sweet ethereal (chloroform-like) smell. It has a melting point of –84.8 °C, a boiling point of 86.7 °C, a Henry's Law constant of 1.03×10^{-2} atm-m^3/mol at 20 °C, a vapour pressure of 7.8 kPa at 20 °C, a water solubility of 1.1 g/l at 20 °C and a log K_{ow} (octanol–water partition coefficent) of 2.29 *(1)*.

The synonyms of TCE include acetylene trichloride, ethinyl trichloride, trichloroethene, TRI, TRIC, 1-chloro-2,2-dichloroethylene, 1,1,2-trichloroethylene, Trilene and Triklone. Its structural formula is *(1)*:



Conversion factors

At 760 mmHg and 20 °C, 1 ppm = 5.465 mg/m^3 and 1 mg/m^3 = 0.183 ppm; at 25 °C, 1 ppm = 5.374 mg/m^3 and 1 mg/m^3 = 0.186 ppm *(2)*.

Production

In 1990, the estimated industrial production of TCE was 131 kilotonnes in western Europe, 79 kilotonnes in the United States and 57 kilotonnes in Japan, compared to 210, 121 and 82 kilotonnes, respectively, in 1980. The estimated annual consumption in these regions is 65–103% of the production levels. No estimates of production and use are available for other parts of the world *(3)*.

Applications and uses

TCE is mainly used for the vapour degreasing and cold cleaning of manufactured metal parts (80–95% of consumption). Other applications include industrial dry cleaning, printing, the production of printing ink, extraction processes, paint production and textile printing *(2–4)*.

In the atmosphere, TCE may react with photochemically produced hydroxyl radicals yielding phosgene, dichloroacetyl chloride, formyl chloride and other

degradation products. Its half-life in the atmosphere varies with latitude, season and concentration of hydroxyl radicals. Reported half-lives for the reaction with hydroxyl radicals range from 1 day to 2½ weeks (in polar regions, the half-life may be as long as several months in winter) *(5,6)*.

Analytical methods in air

Common methods of measuring indoor concentrations of TCE include integrated active and passive sampling methods using tubes packed with a carbon-based sorbent or evacuated SUMMA canisters (passivated canister sampling apparatus), or diffusion samplers such as charcoal badges. Canister sampling involves controlling the flow of air into a pre-evacuated canister. Sorbent tubes and badges retain compounds according to the affinity of the sorbent for that compound. For sorbent or charcoal sampling, the analytes must first be extracted thermally or chemically, then separated using gas chromatography and identified using a detection method such as mass spectrometry *(7)*. Personal exposure studies often use these sorbent-based methods.

Indoor sources and exposure pathways

Inhalation is the main route of exposure for the general population, but ingestion may significantly contribute to total exposure, particularly if drinking-water sources are highly contaminated. Because TCE can volatilize rapidly from surface water *(4,6)*, contaminated water may be an additional source of indoor exposure, through showering or the use of washing machines and dishwashers, for example. Contaminated soil can also contribute to ambient air concentrations of TCE via vapour intrusion (where TCE in soil gas enters homes through cracks in the foundations) *(2,8)*. Dermal exposure can contribute to the total exposure, especially through the use of detergent products or showering *(1,9)*. In a risk assessment study, Fan et al. *(10)* showed that the three most important exposure pathways are water ingestion, dermal absorption when showering and breathing indoor air.

Consumer products

Consumers may be exposed to TCE through the use of wood stains, varnishes, finishes, lubricants, adhesives, typewriter correction fluid, paint removers and certain cleaners, where TCE is used as a solvent *(11)*. Use of these products may result in elevated indoor air concentrations over background, although, as they are expected to be used intermittently rather than constantly, both short-term and long-term average concentrations are likely to be variable.

Groundwater and drinking-water

Groundwater levels are variable and subject to local contamination. In wide-ranging surveys, concentrations have been shown to be mostly low, of the order

of < 0.2–2 μg/l. However, measurements in groundwater related to contaminated sites may show high levels; up to 950 mg/l has been found *(1)*.

Levels of TCE in drinking-water are generally less than 1 μg/l, although higher levels (up to 49 μg/l) have been reported *(1)*. In a survey carried out in Germany during the 1990s, TCE was detected in about 40% of the tested drinking-water samples, with a concentration of more than 1 μg/l for 5.5% of the supplied residents (concentration range < 0.001–21 μg/l) *(6)*. A regular monitoring programme is in place for drinking-water in England and Wales, covering 31 areas. TCE levels were monitored at approximately 2700 sites in 1994. The vast majority of measured TCE levels were below the detection limit (range 0.1–3.0 μg/l), although higher levels (up to 25 μg/l) have occasionally been detected *(1)*. The EPA Groundwater Supply Survey of drinking-water systems nationwide detected TCE in 91 out of 945 water systems in 1984. The median level of the positive samples was about 1 μg/l, with a maximum level of 160 μg/l *(2)*. In Canada, the majority of drinking-water supplies contain less than 0.2 mg/l TCE *(5)*.

Food

The presence of TCE has been demonstrated in a wide range of foodstuffs, and in some exceptional cases high concentrations have been detected. In some countries, the use of TCE as a solvent in the production of foodstuffs has been banned. In total diet studies carried out in the United States, TCE was detected in only a small proportion of the samples *(2,5)*. In the United States, dairy products (particularly butter) and margarine have been found to have high levels of TCE. Levels of 73 μg/kg in butter and margarine were found, while cheese products had an average level of 3.8 μg/kg *(11)*. TCE is lipophilic and has been detected in the breast milk of women living in urban areas, though no quantitative data are available *(2)*. It is possible that this may be leading to a high daily intake for nursing infants.

Indoor air concentrations

Residential concentrations

Indoor concentrations of TCE have been found to be near or below 1 μg/m^3 in many microenvironments where the presence of known sources is uncommon. In several United States cities (New York, Los Angeles, Chicago, Minneapolis, St Paul, Baltimore, Elizabeth and Houston), median indoor residential concentrations ranged from 0.1 to 0.5 μg/m^3; in many cases, standard deviations were of the same order of magnitude as the medians *(12–19)*. Indoor : outdoor ratios in New York and Los Angeles, in a study in a low-income group, were between 1 and 2 at the median and did not have large standard deviations relative to the median (except for New York homes in the winter) *(16)*. This indicates that indoor TCE was probably derived from outdoor sources in the homes in this study. In the United States studies mentioned, outdoor residential median levels ranged

from 0.1 to 0.4 μg/m³ with little variability *(12–19)*. Sampling in different seasons did not show significant differences.

In the European EXPOLIS study, conducted in 1998–1999 using the same methods in six European cities, it was found that in cities with high outdoor residential concentrations such as Athens, Milan and Prague, indoor residential levels were also higher *(20)*. In Athens, the median indoor concentration was 8.2 μg/m³ with a 90th percentile of 22.4 μg/m³, compared with a median of 4.3 μg/m³ outdoors and a 90th percentile of 33 μg/m³. In Milan, the median indoor concentration was 7.7 μg/m³ and the 90th percentile was 21.2 μg/m³, while the median outdoor concentration was 2.3 μg/m³ and the 90th percentile was 8 μg/m³. In Prague, the median indoor concentration was 13.6 μg/m³ and the 90th percentile was 28.9 μg/m³, while the median outdoor concentration was 3.7 μg/m³ and the 90th percentile was 7.7 μg/m³. These indoor levels are likely to be a reflection of the contribution of outdoor sources through infiltration, as the outdoor levels were much higher than in Helsinki, Basel and Oxford. In Helsinki, most of the indoor and outdoor samples were below the detection limit. Basel had similar indoor and outdoor levels to those in Helsinki, while Oxford had slightly higher levels (median 2.1 μg/m³ and 90th percentile 6.6 μg/m³ indoors, and median 2.5 μg/m³ and 90th percentile 4.9 μg/m³ outdoors). The higher indoor (median 7.7–13.6 μg/m³) than outdoor levels (median 2.3–4.3 μg/m³) overall in Milan, Athens and Prague indicate that there may be an additional contribution of indoor sources to indoor TCE concentrations.

A nationwide survey of residences in France (n = 567; monitoring carried out in 2003–2005) found median indoor concentrations of 1 μg/m³; the 95th percentile concentration was 7.4 μg/m³ *(21)*. Indoor concentration in the attached garage (n = 139) was below the detection limit at the median and 12.9 μg/m³ at the 95th percentile, suggesting the presence of indoor sources. Outdoor concentrations (n = 517) were below the detection limit at the median and 2.3 μg/m³ at the 95th percentile.

A study of 25 homes in Shimizu, Japan found indoor geometric mean concentrations of 0.22 μg/m³ (geometric SD = 2.16) in the summer and 0.36 μg/m³ (geometric SD = 1.64) in the winter *(22)*. These were similar to the corresponding outdoor geometric mean concentrations of 0.23 μg/m³ (geometric SD = 2.14) measured in the summer of 2002 and 0.36 μg/m³ (geometric SD =1.61) in winter 2002 *(22)*, indicating that again, infiltration from the outdoors was likely to have been the main source of TCE indoors.

Non-residential microenvironments

A survey of 70 office buildings in the United States (without any reported complaint) found a median TCE concentration of 0.29 μg/m³ with a 95th percentile of 2.6 μg/m³ *(23)*. A study of mechanically ventilated office sector and non-office sector spaces in 20 public buildings in Hong Kong SAR, China found arithmetic

means of 5.6 μg/m³ (SD = 9.6) for offices and 8.8 μg/m³ (SD = 10.7) in non-office areas *(24)*. Other studies of offices, restaurants and stores found TCE median or mean levels below 1 μg/m³, although there was a high degree of variability in some cases *(25–27)*. In general, it appears that, for the most part, TCE in non-residential indoor environments is associated with infiltration from outdoors, as common indoor environments are unlikely to have sources of TCE in amounts that would contribute enough to the indoor concentration to result in significantly elevated levels compared to outdoors. Studies have found that most non-industrial areas do not have significantly high outdoor levels compared to industrial areas.

Modelled air concentrations of TCE near different types of vapour degreasing machine have been estimated to range from around 5 mg/m³ for newer, closed-loop machines to over 1000 mg/m³ for older, open-top machines. In Germany, levels of TCE in degreasing applications based on occupational personal air concentrations in the 1990s were found to be around 20–50 mg/m³ on average *(28)*.

Ambient air

Concentrations of TCE in ambient outdoor air may fluctuate widely over relatively short periods of time, depending on the strength of the emission source, variations in wind direction and velocity, and scavenging and photodecomposition *(5)*. Arithmetic mean rural concentrations in Canada were found to be 0.02 μg/m³ with a maximum value of 4 μg/m³, based on passive month-long measurements in 2001 and 2002 *(29)*.

Short-term measurements made during peak traffic hours on busy roads in industrial, commercial, residential and central business districts in Hong Kong SAR, China gave arithmetic mean TCE concentrations of 48.5 μg/m³ (SD = 77.8), 3.6 μg/m³ (SD = 3.4), 0.4 μg/m³ (SD = 0.5) and 1.3 μg/m³ (SD = 1.8), respectively *(30)*. These patterns indicate that areas of heavy industry have significantly higher, although more variable, concentrations of TCE, probably due to the presence of high-emitting sources. Residential and non-industrial areas where few sources are present have much lower concentrations. Based on results from the European EXPOLIS study in Athens, Milan and Prague, it is likely that small industry sources are either mixed in with residential and business areas or that heavy industry is near these areas. Non-residential indoor environments in Athens, Milan and Prague were found to have similar TCE levels to indoor home environments. Median workplace concentrations were 6.4 μg/m³ in Athens, 4.7 μg/m³ in Milan and 4.4 μg/m³ in Prague *(20)*.

Toxicokinetics and metabolism

Identification of studies

Considering the possible overlaps in the relevant evidence on health effects of trichloroethylene, the search of the literature supporting the "Toxicokinetics and

metabolism" and "Health effects" sections was conducted in one process. The electronic searches were made in PubMed between August and September 2008, with an update in 2009. The keywords used were: "trichloroethylene" and "health effects" or "risk assessment" or "metabolism/biotransformation/kinetics". We selected all relevant papers on this subject. Around 100 publications were selected; 23% concerned the metabolism of TCE and mostly the development of PBPK models, 16% focused on molecular mechanisms and mode of action, and 29% were related to toxicological tests in mammals. One third discussed reproductive and developmental effects while 25% concerned human studies, mostly the exposure of workers and pregnant women in the general population. Finally, two reviews on toxicological effects, three on carcinogenic risk in human and two on risk assessment were also selected.

A complementary Internet search was made in August 2008 on toxicological databases (hazardous substances databank, TOXNET) and on the web site of international or national health assessment agencies, including WHO, the European Commission, IPCS, ATSDR, Health Canada, the French Agency for Environmental and Occupational Health Safety (Affset) and USEPA. Twelve reports from these agencies, published between 1985 and 2009, were selected.

Toxicokinetics

Two update reviews of the pharmacokinetics of TCE have recently been published *(31,32)*.

Absorption

In humans and in animals, TCE is readily absorbed via the oral, inhalation and dermal routes.

Because TCE is an uncharged, nonpolar and highly lipophilic molecule, gastrointestinal absorption is extensive and occurs by passive diffusion *(31)*.

In humans, TCE is known to be highly and rapidly absorbed by inhalation (25–55%) *(33)*, with a high uptake during the first few minutes and steady-state blood levels reached within 2 hours. This high absorption rate is due to the high blood–air partition coefficient, which ranges from 9 to 15 *(34)*. The absorption after inhalation is also high in animals, but significant differences in blood–air partition coefficient exist between species *(31)*.

TCE can also penetrate intact human skin. Four human male volunteers had TCE blood concentrations of 2 mg/l immediately following the immersion of one hand in TCE for 30 minutes. Levels fell to 0.34 mg/l 30 minutes after the end of the immersion period and to 0.22 mg/l after 60 minutes *(35)*.

Distribution

After absorption, TCE is widely distributed in the body via the circulatory system. Because of its high liposolubility, it is predominantly found in adipose tis-

sue and then in the liver, kidneys, cardiovascular system and nervous system *(2)*. TCE crosses the blood–brain barrier and the placenta *(36)*. It has been shown in lactating rats that TCE and its metabolite trichloroacetic acid are excreted in milk. In goats, TCE and its metabolite trichloroethanol were found to be transferred to milk to a slight degree only *(37)*.

Biotransformation

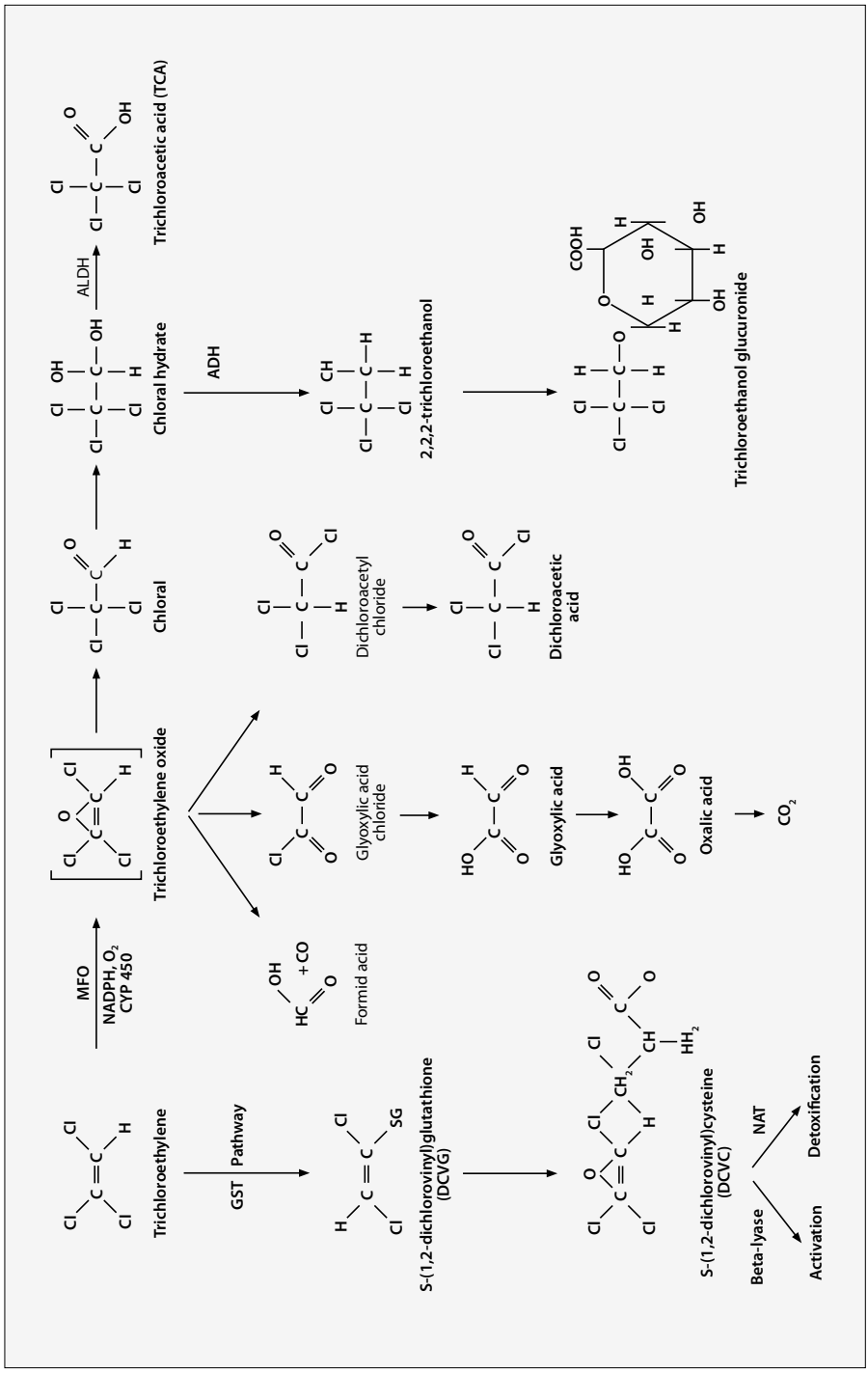
In humans, 40–75% of the retained dose of inhaled TCE is metabolized. The metabolic pathways are qualitatively similar in all species. TCE is metabolized to multiple metabolites either locally or in systemic circulation (e.g. in the liver and by Clara cells in the lung). Many of these metabolites are thought to have toxicological importance *(38)*. The general pattern of enzymatic metabolism occurs through two main pathways: oxidation via the microsomal mixed-function oxidase system (CYP450) and, to a lesser extent, conjugation with glutathione *(32)*.

- TCE is principally and rapidly transformed by CYP 2E1 *(39)* into an epoxide intermediate, which spontaneously rearranges to trichloroacetaldehyde and then chloral hydrate. Chloral hydrate acts as a substrate for alcohol dehydrogenase and chloral hydrate dehydrogenase, leading to the formation of trichloroethanol and trichloroacetic acid, respectively. The main metabolites, which are primarily present in the urine, are therefore trichloroethanol, its glucuronide conjugate and trichloroacetic acid. Metabolism appears to be qualitatively identical, irrespective of the exposure route *(2)*.
- Other minor metabolites of TCE have been identified, including the mercapturic acid N-acetyl-S-(dichlorovinyl)-L-cysteine (DCVC), which is formed in the kidneys from the glutathione conjugate of TCE (previously formed in the liver as a minor biotransformation product). The presence of DCVC in the urine has been demonstrated in rats and also in workers exposed to TCE *(37)* (Fig. 8.1).

The metabolism of TCE is quantitatively dependent on the concentration and species tested: it is concentration-dependent in rats but not in mice. In humans, no saturation has been demonstrated. As a consequence of differences in blood flow and overall metabolic rate, species differences exist in the fraction of administered dose of TCE that is available for conversion to toxic metabolites in the target organs *(31)*. In mice, oxidative metabolites are formed in greater quantities than glutathione conjugate metabolites, and dichloroacetic acid is produced to a very limited extent relative to trichloroacetic acid, while most S-(1,2-dichlorovinyl)glutathione (DCVG) is converted into DCVC *(40)*.

TCE is well metabolized by human hepatocytes in culture, with a K_m of 266 (± 202) ppm and a V_{max} of 16.1 (± 12.9) nmol/hour per 10^6 viable hepatocytes. Lipscomb et al. *(41)* predicted a V_{max} of approximately 1400 nmol/hour per gram of human liver.

Fig. 8.1. Metabolism of trichloroethylene



Sources: ATSDR *(2)*; Chiu et al. *(32)*.

The link between the various metabolites of TCE and diverse types of toxicity is known to be highly complex, making understanding of the toxicological mechanisms of action more complicated. Animal-to-human extrapolation is a source of a high level of uncertainty *(42)*. There is inconclusive evidence suggesting that the glutathione biotransformation route, leading to DCVC production, is more important in humans than in rodents *(43)*.

When ten volunteers were exposed to 250–380 ppm of TCE for 160 minutes, 16% of the retained TCE was eliminated through respiration after exposure. Trichloroacetic acid excretion in females was 2–3 times more than in males for the first 24 hours. However, twice as much trichloroethanol was excreted in males. These observations suggest a sex difference in human metabolism (Nomiyama & Nomiyama 1971, cited in HSDB *(36)*).

Elimination

In humans and animals, non-metabolized TCE can be eliminated via expired air (11–40%). The main metabolites are eliminated by the kidneys: urinary elimination of trichloroethanol and trichloroacetic acid is complete 5 and 13 days, respectively, after the end of exposure *(35,44)*. In humans, the half-times for renal elimination of trichloroethanol and its glucuronide are about 10 hours. Urinary excretion of trichloroacetic acid is slower, with a reported half-time of about 52 hours *(2)*. Male volunteers were administered chloral hydrate in three separate experiments. Chloral hydrate, dichloroacetic acid, trichloroacetic acid, and trichloroethanol and its glucuronide were measured in blood and urine over a 7-day period. Trichloroacetic acid had the highest plasma concentration and the largest area under the curve of any metabolite. The trichloroacetic acid elimination curve displayed an unusual concentration–time profile that contained three distinct compartments. This complex elimination pattern may result from the enterohepatic circulation of trichloroethanol glucuronide and its subsequent conversion to trichloroacetic acid, as shown in rats *(45)*.

Biomarkers of human exposure

Biomonitoring of TCE is possible by measuring levels of the parent compound or its main metabolite, trichloroacetic acid, in expired air, blood and urine.

Several studies have demonstrated a correlation between levels of TCE in ambient air and in exhaled air *(2)*. Following inhalation exposure to TCE, 10–11% of the absorbed dose is found in expired air as TCE and 2% is eliminated as trichloroethanol.

A linear correlation has been reported between the inhalation exposure of TCE and the urinary levels of trichloroethanol and trichloroacetic acid. In a kinetics study in male volunteers, trichloroacetic acid had the highest plasma concentration and the largest area under the curve of any metabolite *(45)*. Because urinary trichloroacetic acid has a longer half-life than trichloroethanol, it bet-

ter reflects long-term exposure, whereas urinary trichloroethanol reflects recent exposure *(2)*. The American Conference of Governmental Industrial Hygienists adopted biological exposure indices for TCE based on blood concentrations of free trichloroethanol and trichloroacetic acid and trichloroethanol in urine *(46)*. It should be noted, however, that there is great inter-individual variability in the concentrations of trichloroethanol and trichloroacetic acid in urine and that trichloroacetic acid is not specific to TCE exposure.

Although some studies have shown that protein and DNA adducts may form with chlorinated hydrocarbons *(37)*, their application has not been validated sufficiently to justify their use as biological markers of exposure *(47)*. Some researchers have developed methods to interpret biomarkers by reconstructing human population exposures *(48,49)*. These methods are based on PBPK models (see below) combined with Monte Carlo or Bayesian analysis and estimate TCE environmental concentrations based on known concentrations in blood. This approach involves the interpretation of human biomonitoring data and a possible comparison with health-based exposure guidelines.

Physiologically based pharmacokinetic modelling

Efforts to develop physiologically based pharmacokinetic (PBPK) models have led to an improved assessment of TCE. Several PBPK models have been proposed. They focus on descriptions of both TCE and its major oxidative metabolites in humans (trichloroacetic acid, trichloroethanol and its glucuroconjugate) (see Chiu et al. *(32)* for additional discussion). Several families of PBPK model are available:

- Fisher models permit the modelling of liver cancer risks following oral and inhalation exposure of TCE and the formation of metabolites in the liver in humans and mice. None of these models consider renal metabolism (and, therefore, the glutathione pathway in particular), which may play an important role in toxic signs in humans *(50–54)*.
- The Clewell model is more complex than the Fisher models, since it includes sub-models for the main metabolites and for the three target organs demonstrated during toxicity studies in animals (lung for trichloroacetaldehyde, kidney for dichlorovinylcysteine and liver for trichloroacetaldehyde, di- and trichloroacetic acids, trichloroethanol and its conjugate). This model takes into account inhalation and oral exposure, along with hepatic and renal metabolism *(55)*.
- The Bois model calibrates the existing models of Fischer and Clewell with new toxicokinetic data and includes a Bayesian statistical framework to bring in issues on variability and uncertainty for each parameter *(56,57)*. More recently, other researchers have shown that a combination of Bayesian approaches and PBPK analysis provides better predictions and yields an accurate characterization of the uncertainty in metabolic pathways for which data are sparse *(58)*.

- Combining the Fischer and Clewell models, and considering the reassessment of the parameters of these models conducted by Bois et al. *(56,57)* using Bayesian methods, the United States Air Force proposed, in 2004, a harmonized model for use in mice, rats and humans *(32,59)*.

PBPK models have largely been applied in risk assessment to predict dose metrics, toxicity or guideline values. Yoon et al. *(60)* found that liver-only metabolism may be a reasonable simplification for PBPK modelling of TCE to predict dose metrics. Simmons et al. *(61)* explored the relationship between measures of internal doses of TCE and neurotoxic outcomes in rats. Another application is based on the time course of TCE in blood and brain of rats and humans to adjust duration for acute guidelines in place of the Haber's law *(62–64)*. Hacks et al. *(65)* used a Bayesian approach to reduce uncertainty in dose metric prediction of TCE and its metabolites (particularly trichloroacetic acid and trichloroethanol). More recently, Evans et al. *(66)* examined the question of whether the presence of trichloroacetic acid in the liver is responsible for TCE-induced hepatomegaly in mice, and concluded that oxidative metabolites, in addition to trichloroacetic acid, are necessary contributors.

Despite their continuous development, none of these PBPK models currently incorporates all exposure routes or all the possible toxic effects. Similarly, the dose measurement to be used in these models is not clearly explained, i.e. whether it should be area under the curve, cumulative dose or maximum concentration. The development of more complex models is notably linked to advances in scientific knowledge concerning understanding of the mechanism(s) of toxic action of TCE.

Health effects

Effects in experimental animals and in vitro test systems

Non-carcinogenic effects

In animals, the major effect of acute exposure includes a state of excitation followed by CNS depression and drowsiness. This depression is marked by a loss of reflexes and motor coordination, potentially progressing to coma. The LC_{50} values are 142 g/m^3 (1 hour) and 71 g/m^3 (4 hours) in rats and 46 g/m^3 (4 hours) in mice, indicating a low acute inhalation toxicity. A transient hepatic toxicity has been observed in rodents. A specific pulmonary toxicity (to Clara cells) has been demonstrated in mice and a transient specific nephrotoxicity is demonstrated when the metabolism is saturated in rats *(35,44)*.

Effects on the CNS have also been demonstrated during subchronic and chronic inhalation exposure. In rats, a NOAEL of 2700 mg/m^3, based on an increase of latency in visual discrimination tasks, was identified after 18 weeks of inhalation exposure *(67)*. In a 16-week study in rats, brainstem auditory-evoked response potentials were depressed at test concentrations as high as 8640 and

17 280 mg/m^3 *(68)*. Electroencephalograph changes have also been reported in rats exposed to up to 50 ppm for 6 weeks *(69)*. In rabbits, neuro-ophthalmological reversible modifications were observed during a 12-week period of inhalation exposure at 1890 and 3780 mg/m^3 *(70)*. Based on the hypothesis that organic solvents can promote noise-induced hearing loss, Vyskocil et al. *(71)* reviewed the effects of low-level exposure to TCE on the auditory system. In rats, TCE affects the auditory function mainly in the cochlear mid- to high-frequency range, with a LOAEL of 2000 ppm. Supra-additive interaction after exposure to noise and TCE has been reported *(71)*. A recent animal study was conducted to determine whether TCE exposure is neurotoxic to the striatonigral dopamine system that degenerates in Parkinson's disease. The study showed that oral administration of TCE for 6 weeks leads to a complex 1-mitochondrial impairment in the midbrain and a striatonigral fibre degeneration and loss of dopamine neurons *(72)*.

Transient hepatic hypertrophy has also been observed, but the results of studies are equivocal and its toxicological significance is not clear. Inhalation exposures to 2000 ppm TCE show elevated plasma alanine and aspartate aminotransferase activities and liver histopathological abnormalities in mice. At the same dose, TCE significantly upregulates PPARα *(39)*. Sano et al. *(73)* demonstrated distinct transcriptional profiles and differences in biological pathways between rats and mice, suggesting species differences in liver toxicity.

An increase in kidney weight has been demonstrated in rats, but without any particular associated histological changes *(74)*. Megalonucleocytosis has been observed and a NOAEL has been defined at 115 mg/m^3 *(75)*. The relative importance of metabolism of TCE by the CYP450 and glutathione conjugation pathways in the acute renal and hepatic toxicity of TCE was studied in isolated cells and microsomes from rat kidney and liver. Increases in cellular glutathione concentrations increased TCE cytotoxicity in kidney cells but not in hepatocytes, consistent with the role of glutathione conjugation in TCE-induced nephrotoxicity. In contrast, depletion of cellular glutathione concentrations moderately reduced TCE-induced cytotoxicity in kidney cells but increased cytotoxicity in hepatocytes, consistent with the different bioactivation pathways in kidney and liver *(76)*. The involvement of CYP450 in TCE-induced hepatotoxicity was also studied in mice and its major role in the hepatotoxicity of TCE confirmed *(39)*. Recently, Khan et al. *(77)* showed that TCE causes altered carbohydrate metabolism and suppresses the antioxidant defence system in rats. These results are consistent with the hypothesis that TCE induces oxidative stress in kidney and other tissues.

Immune disorders have been observed in rats *(78,79)*. A decline of CD4+ in T lymphocytes was observed after intradermic administration of TCE, but no significant concentration differences in IFN-gamma and IL-4 were found between TCE-treated animals and controls *(78)*. Other animal experiments suggest that immunotoxicity is mediated via haptenization of macromolecules and that

haptenized proteins may act as neo-antigens that can induce humoral immune response and T-cell-mediated hepatitis in mice. Further observations suggest that TCE promotes inflammation in the liver, pancreas, lung and kidney, which may lead to SLE-like disease *(80)*. DCA could be involved in the immune disorders and hepatotoxicity induced by TCE *(81,82)*.

Moreover, Tang et al. *(83)* recently found that TCE can induce non-dose-related hepatitis classified as a delayed-type hypersensitivity at low doses in guinea-pigs exposed via intradermal injection (below the dose causing liver injury) and with different histopathological changes. TCE exposure in mice generates a time-dependant increase in antibodies specific for liver proteins in mice, upregulates the methionine/homocysteine pathway in the liver, and alters the expression of selective hepatic genes associated with immunity *(84)*. Moreover, TCE enhances histamine release from antigen-stimulated mast cells and inflammatory mediator production *(79)*. Other researchers suggest that protein oxidation (carbonylation and nitration) could contribute to TCE-induced autoimmune response because an increase in oxydatively modified proteins is associated with significant increase in cytokines. These first results observed in mice require further study *(85)*.

TCE could be skin irritant: a recent study investigating acute and cumulative TCE topical treatment in BALB/c hairless mice showed skin reaction (erythema and oedema) and histopathological changes (hyperkeratosis and inflammatory cell infiltrates) *(86)*.

Based on in vivo and in vitro studies, the US National Research Council *(87)* concluded that exposure to TCE disrupts spermatogenesis, reduces male fertility and the fertilization capacity of spermatozoa, and reduces the capacity of oocytes to be fertilized in females. Studies conducted in male Wistar rats exposed by inhalation to 376 ppm of TCE for 12 or 24 weeks *(88,89)* demonstrated a significant reduction in the number and motility of spermatozoa and in steroid enzyme activity (dehydrogenases), with a reduction of testosterone levels in the sperm. This was associated with a reduction of absolute testicular weight and histopathological changes. The fertility of these male rats was reduced when mating was performed with untreated females. Testicular cholesterol was elevated in exposed rats, suggesting that TCE acts on the biosynthesis of testosterone in the testis. Histological changes have also been shown (in spermatogonia and spermatids, seminal tubes and Leydig cells) but the reversibility of the effects has not been studied. A study in mice exposed to 1000 ppm for 1–6 weeks did not demonstrate any effects on testis or sperm *(90)* but mating with non-exposed females resulted in a significant decrease in the rate of fertilized oocytes after 2 and 4 weeks. Furthermore, an in vitro assay demonstrated a reduction in the number of spermatozoa per oocyte after treatment with 0.1–10 µg/l chloral hydrate or trichloroethanol. This suggests that the metabolites (in particular chloral hydrate) were responsible for the reproductive toxicity of TCE. More recently, Kan

et al. *(91)* showed epithelial damage (vesiculation in the cytoplasm, disintegration of basolateral cell membranes and sloughing of epithelial cells) in the epididymis of mice exposed to 1000 ppm TCE for 1–4 weeks. Further experiments *(92,93)* demonstrated that TCE could also cause reproductive toxicity in female rats, with a decrease in spermatozoon penetration and oocyte fertilization and reduced membrane-binding protein in female rats treated with TCE (2 weeks' administration of drinking-water containing 0.45% TCE). These effects also appear to be dependent on metabolic activation by CYP2E1 (without metabolite(s) being involved) and on glutathione conjugation to DCVC *(94)*. The real impact of the biological effects observed on the reproductive function of the animals is not known, nor is the transposability of these effects to human reproductive function. Finally, these observations suggest that enzyme induction and oxidative metabolism may play a role in the reproductive toxicity of TCE. Oxidative metabolites of TCE are formed in the mouse epididymis, resulting in epididymal damage, and at systemically toxic high doses TCE may adversely affect the maturation of sperm and decrease sperm motility *(95)*. Lamb & Hentz consider that protection against systemic toxicity should also protect against adverse effects, including male reproductive toxicity *(95)*.

One study has suggested the possibility of an increased incidence of malformations in rat pups after oral exposure via drinking-water. An increase in the incidence of cardiac and eye malformations was observed in pups from dams exposed to 0.18 and 132 mg/ kg body weight per day before and during gestation (3 months before or 2 months before and during pregnancy) or only 132 mg/kg body weight per day in dams exposed only during gestation, without maternal toxicity *(33)*. However, a recent evaluation by Williams & Desesso *(96)* pointed out the maternal toxicity associated with this birth defect. The mechanism of action is not known but it may involve metabolism by CYP450 2E1 and dichloroacetic and trichloroacetic acids. No malformation has been reported in inhalation studies in rats and other oral animal studies have not demonstrated conclusive results *(33,87,97)*. A recent study, in which mice were exposed to 31 mg/kg body weight per day via drinking-water from gestational day 1 to postnatal day 42, showed that developmental and early life exposure of TCE could modulate the immune function of pups and may be associated with neurodevelopmental disorders *(98)*.

A summary of relevant animal inhalation studies for subchronic and chronic exposures to TCE, indicating derived NOAELs and LOAELs, is shown in Table 8.1.

Carcinogenic effects

Exposure to TCE was responsible for an increased incidence of liver tumours in male Swiss mice and B6C3F1 mice of both sexes exposed by the inhalation route to 600 ppm for 78 weeks. Pulmonary tumours were also increased in fe-

male B6C3F1 and male Swiss mice at 600 ppm, but not among the male B6C3F1 mice *(75)*. Other studies have demonstrated a significant increase in pulmonary adenocarcinomas in female ICR mice exposed to 150 or 400 ppm for 104 weeks *(100)*. In male Sprague-Dawley rats, inhalation exposure to 600 ppm of TCE for 104 weeks led to a dose-dependent increase in Leydig cell tumours in the testis and a marginal increase in renal tumours (adenocarcinomas of the renal tubules). Finally, in mice, rats and hamsters exposed to 100 and 500 ppm TCE for 18 months, the only significant increase in tumour incidence was for malignant lymphomas in female mice *(75)*. The results of experimental studies are presented in Table 8.2.

The metabolism of TCE doubtless plays a very important role in its mechanism of carcinogenic action. Metabolic pathways have largely been described *(33,101–103)*. The research to date indicates that TCE-induced carcinogenesis is complex, involving multiple carcinogenic metabolites acting in various ways. Past explanations, such as the hypothesis linking mouse liver tumours to peroxisome proliferation, are not consistent with the whole of the data, and more complex hypotheses have been formulated *(38)*. A plausible mode of action is that TCE induces liver tumours through trichloroacetic acid and DCA modifying the cell signalling systems that control cell division rate and cell death *(103–105)*. This hypothesis suggests that humans are likely to be much less responsive than mice and that carcinogenic effects are unlikely to occur at low environmental exposures. The induction of pulmonary tumours in mice may be linked to the fact that Clara cells rapidly metabolize TCE into chloral hydrate, via CYP450 2E1, leading to pulmonary accumulation of this metabolite, which ultimately produces cell changes and compensatory proliferation. But other mechanisms of action may be involved, particularly since chloral hydrate is probably genotoxic and, at high doses, clastogenic. In rats, Clara cells are capable of metabolizing chloral hydrate into trichloroethanol. In humans, the capacity of the lung to transform TCE into chloral hydrate is thought to be negligible and, consequently, the mechanism of pulmonary carcinogenesis demonstrated in mice may be specific to mice.

Finally, renal tumours in male rats may be linked to cytotoxicity and persistent cell regeneration. Conjugation to glutathione and the involvement of beta-lyase in the renal tubules may lead to the formation of nephrotoxic and probably genotoxic reactive metabolites, in particular DCVC and DCVG *(101)*. Studies have demonstrated that TCE induces mutations in the VHL (Von Hippel-Lindau) tumour suppressor gene in the cells of renal carcinomas in patients with this cancer *(106,107)*, but Charbotel et al. *(108)* did not confirm the association between the number and type of VHL gene mutations and exposure to TCE.

A second mechanism may involve increased secretion of formic acid, leading to a disruption in the detoxification mechanism by methionine. The mechanism of carcinogenic action leading to the development of renal tumours in rats is less

Table 8.1. A review of animal inhalation studies for subchronic and chronic exposure

Reference	Species	Duration	Concentrations
Kjellstrand et al. *(99)*	Mice	Subchronic (30 days)	0–37–75–150–300 ppm
Xu et al. *(90)*	Mice	Subchronic (1–6 weeks)	0–1000 ppm
Kan et al. *(91)*	Mice	Subchronic (1–4 weeks)	0–1000 ppm
Arito et al. *(69)*	Rats	Subchronic (6 weeks)	0–50–100–600 ppm
Maltoni et al. *(75)*	Rats	Chronic (104 weeks)	0–100–300–600 ppm
Kulig *(67)*	Rats	Chronic (18 weeks)	0–500–1000–1500 ppm
Rebert et al. *(68)*	Rats	Chronic (12 weeks)	0–1600–3200 ppm
Blain et al. *(70)*	Rabbits	Chronic (12 weeks)	0–350–700 ppm
Kumar et al. *(88)*	Rats	Chronic (12 weeks and 24 weeks)	0–376 ppm
Kumar et al. *(89)*	Rats	Chronic (12 weeks and 24 weeks)	0–376 ppm
Carney et al. *(97)*	Rats	Gestational (gestational days 6–20)	0–50–150–600 ppm

[a] The LOAEL is the lowest dose causing an adverse effect in animals in the experiment (from a statistically significant point of view). The NOAEL is the tested dose just below the LOAEL (the highest dose not causing any adverse effects in the experiment).

clearly determined but its transposability to humans is questionable. There is no tested hypothesis to take into account the mechanistic aspects of the induction of malignant lymphomas in mice and testis tumours in male rats. These considerations, and the effects observed in humans, justify a cautious attitude regarding the extrapolation to humans of results observed in animals.

In conclusion, despite the numerous limitations to confident interpretation of some of the data (e.g. the response of animals differs depending on sex for renal tumours and depending on species for hepatic and pulmonary tumours), animal evidence is deemed sufficient for evaluating the carcinogenic effect of TCE. The European Commission's risk assessment report on TCE concludes that studies provide clear evidence that TCE is carcinogenic in rats and mice through oral and inhalation exposure *(1)*.

Critical effect	LOAEL & NOAEL[a]
Liver and kidney: change in liver and kidney weight (more pronounced in males)	LOAEL = 150 ppm NOAEL = 75 ppm
Significant decrease in the rate of fertilized oocytes after 2 or 4 weeks	LOAEL = 1000 ppm No NOAEL
Epithelial damage in the epididymis	LOAEL = 1000 ppm No NOAEL
CNS: electroencephalograph changes (wakefulness-sleep periods and heart rate)	LOAEL = 50 ppm No NOAEL
Kidney: megalonucleocytosis	LOAEL = 300 ppm NOAEL = 100 ppm
CNS: increase of latency in visual discrimination tasks	LOAEL = 1000 ppm NOAEL = 500 ppm
CNS: depression of brainstem auditory-evoked response potentials	LOAEL = 1600 ppm No NOAEL
CNS: neuro-ophthalmological modifications	LOAEL = 350 ppm No NOAEL
Testicular toxicity: changes in testosterone and testicular cholesterol levels; decrease in 17β-hydroxysteroid dehydrogenase and glucose 6-P-dehydrogenase activity, and sperm (number and motility)	LOAEL = 376 ppm No NOAEL
Testicular toxicity: reduction in absolute testicular weight; changes in testicular enzyme activity associated with spermatogenesis and germ cell maturation; histopathological changes showing depletion of germ cells and spermatogenic arrest	LOAEL = 376 ppm No NOAEL
Maternal toxicity: 22% decrease in body weight (gestational days 6–9) Fetal toxicity: none	LOAEL maternal toxicity = 600 ppm NOAEL maternal = 150 ppm NOAEL fetal = 600 ppm

Genotoxicity

In Europe, TCE has been classified since 2001 as mutagenic category 3 (risk phrase R68) under Directive 67/548/CEE. Several reviews on the mutagenicity of TCE are available in the literature *(2,3,110)*. TCE seems to be genotoxic in vitro: the Ames test and in vitro mouse lymphoma test have shown a weak positive response with activation, but this characteristic is equivocal in vivo. A recent paper by Hu et al. *(111)* assesses the in vitro genotoxic effects of TCE and the underlying mechanisms using human HepG2 cells: TCE exposures (0.5–4 mM) caused positive response in comet assay and micronuclei assay. These results suggest that TCE causes DNA strand breaks and chromosome damage in hepatocytes. In another study evaluating the in vivo genotoxicity of TCE (99.5% purity) by inhalation (500–1000–2000 ppm) and DCVC (> 95% purity) by oral gavage (1–10 mg/kg), using the comet assay to assess DNA breakage in the proximal tu-

Table 8.2. Review of inhalation carcinogenic studies in animals

Reference	Species & strain	Duration
Henschler et al. *(109)*	NMRI mice (2 sexes)	78 weeks, 7 hours/day, 5 days/week
	Syrian hamsters (2 sexes)	78 weeks, 7 hours/day, 5 days/week
	Wistar rats (2 sexes)	78 weeks, 7 hours/day, 5 days/week
Fukuda et al. *(100)*	ICR mice (females)	104 weeks, 7 hours/day, 5 days/week
	Sprague-Dawley rats (2 sexes)	104 weeks, 7 hours/day, 5 days/week
Maltoni et al. *(75)*	Sprague-Dawley rats (2 sexes)	104 weeks, 7 hours/day, 5 days/week
	B6C3F1 mice (2 sexes)	78 weeks, 7 hours/day, 5 days/week
	Swiss mice (2 sexes)	78 weeks, 7 hours/day, 5 days/week

Source: WHO *(37)*.

bules of kidneys, rats were exposed at dose levels in excess of those that produced renal tumours. TCE gave a clearly negative response in the assay at all dose levels. DCVC gave a negative response at the lower dose level. At the higher dose level, there was limited evidence of DNA damage in a small number of animals. The authors suggest that the mechanism for induced renal tumours is non-genotoxic *(112)*.

Finally, while the available data on genotoxicity do not show a consistent pattern, the results indicate that TCE has a weak genotoxic action causing numerical chromosomal aberrations (aneuploidy) in vivo and probably DNA strand breaks in hepatocytes in vitro.

Currently, the various hypotheses suggested do not enable accurate identification of the key events responsible for the development of cancers at different sites (lungs, liver, kidneys, etc.). The ambiguity concerning the role of active metabolites, and the various mechanisms of action and effects, lead to a high level of caution when transposing animal data to humans (differences in sensitivity, quantitative differences in kinetics between species and as a function of exposure levels) *(38)*.

In conclusion, the mechanism of carcinogenic action of TCE can be attributed to numerous mechanisms, involving both non-genotoxic and genotoxic phe-

Concentrations	Tumour incidence
0–100–500 ppm (purified TCE without epoxide)	Female lymphomas: 9/29, 18/28, 17/30
0–100–500 ppm (purified TCE without epoxide)	No increase in tumour incidence
0–100–500 ppm (purified TCE without epoxide)	No increase in tumour incidence
0–50–150–450 ppm (99.8% purity, presence of benzene and epichlorhydrin)	Pulmonary adenocarcinomas: 1/49, 3/50, 8/50, 7/46
0–50–150–450 ppm (99.8% purity, presence of benzene and epichlorhydrin)	No increase in tumour incidence
0–100–300–600 ppm (99.9% purity, presence of benzene and epichlorhydrin)	Male renal tubuli adenocarcinomas only at 600 ppm (4/130 vs 1/130 in control group) Leydig cell tumours: 1/135, 16/130, 30/130, 31/130
0–100–300–600 ppm (99.9% purity without epoxide)	Female pulmonary adenomas: 4/90, 6/90, 10/90, 15/90 Female hepatomas: 3/90, 4/90, 4/90, 9/90 Male hepatomas: 14/90, 19/90, 27/90, 21/90
0–100–300–600 ppm (99.9% purity without epoxide)	Male pulmonary adenomas and carcinomas: 10/90, 11/90, 23/90, 29/90 Male hepatomas: 4/90, 2/90, 8/90, 13/90

nomena. It is thus prudent to consider that TCE can induce a risk of cancer in humans based on a non-threshold hypothesis *(42)*.

Unit risk values based on animal data have been estimated using the linearized multistage model on carcinogenicity data from mice and rats and using the most sensitive tumour type for which there is sufficient evidence. Unit risk values were 9.3×10^{-8} per μg/m^3 and 1.6×10^{-7} per μg/m^3 for pulmonary adenomas in B3C6F1 mice and Swiss mice, respectively, and 4.3×10^{-7} per μg/m^3 for Leydig cell tumours in rats. The most protective unit risk (4.3×10^{-7} per μg/m^3) was used to derive health-based guideline values for TCE in air in Europe *(37)*.

Effects in humans

Non-carcinogenic effects

In humans, the main target following the inhalation of high concentrations of TCE is the CNS, as is observed in animals. Neurological damage, especially affecting the optic and trigeminal nerves, has been reported following accidental exposure.

The acute neurological effects of TCE may be more related to maximum blood concentrations than to "area under the curve". In rats, the peak TCE concentration inducing toxicity appears to be higher than in humans, suggesting

that humans are more sensitive than animals for these neurological effects *(42)*. The neurological effects have been observed at concentrations from 270 mg/m^3 (changes in visual and auditory potentials) to approximately 600–1000 mg/m^3 (decreased psychomotor performances) over several hours *(37)*. Cardiac effects (ventricular fibrillation) may also cause death following massive exposure *(42)*. A recent accidental inhalation of TCE during the cleaning of a metal-degreasing machine produced a reversible kidney injury (urinary proteins and enzymes 7 and 74 hours after exposure) in a 54-year-old man. TCE and trichloroacetic acid had peak blood concentrations at 11 and 62 hours after poisoning, respectively *(113)*. Another case report showed acute liver and kidney failure followed by severe brain oedema and death in a 27-year-old man, probably caused by abuse of glue containing TCE *(114)*.

Effects on the CNS have also been demonstrated during chronic inhalation exposures. The majority of studies in humans describe the symptoms following acute exposure, but these are often of inadequate quality (absence of data on exposure or on confounding factors). More discrete neurological effects such as motor incoordination have also been observed for exposures of 87, 60 and 38 mg/m^3, respectively *(102)* but there is no convincing evidence of TCE-induced hearing losses in workers. No studies on ototoxic interaction after combined exposure to noise and TCE have been identified in humans *(71)*. Analysis of a cluster of 30 workers with neurological disease who were chronically exposed to TCE showed that the 3 workers with workstations nearest the TCE source had Parkinson disease. The authors suggest that TCE is a probable risk factor for Parkinsonism *(72)*.

Renal and pulmonary damage in humans following TCE exposure is absent or very slight, but transient effects on the liver have been observed *(37)*. Levels of total cholesterol and high-density lipoprotein cholesterol increased slightly with dose, but without modification of serum enzyme activity. It was suggested that exposure to TCE can influence hepatic function *(115)*. However, all the studies suffer from major methodological limitations, particularly in terms of characterization of exposures. In addition, individuals exposed to TCE were also exposed to other solvents.

Some authors suggest that TCE induces and exacerbates autoimmunity. This is supported by animal experimentations and observations of SLE and other immunological disorders in occupationally exposed human *(82)*. However, idiosyncratic generalized skin disorders complicated by hepatitis have rarely been observed in populations occupationally exposed to TCE in factories where TCE metabolites could extensively accumulate (urinary trichloroacetic acid concentrations from 318 to 1617 mg/l) *(116)*. This is consistent with a recent study by Xu et al. *(117)* in which TCE induced hypersensitivity dermatitis and liver dysfunction in Chinese workers exposed to 18–683 mg/m^3 for an average of 38.2 days (range 5–90 days). Liu et al. *(118)* found autoantibodies in sera collected

from patients who (had) suffered from TCE-induced dermatitis. These antibodies could perhaps be used to understand underlying mechanisms in the immunotoxicity of TCE.

The effect of inhaled TCE on fertility in humans has not been studied. The most recent studies have demonstrated a number of modifications in endocrine function, revealed by measurement of steroid hormones in particular, with changes observed following exposure to 60 mg/m^3 TCE *(119–121)*, but the toxicological significance of these observations has not been investigated.

Epidemiological studies have been carried out in occupational environments to investigate any link between exposure to degreasing solvents (including TCE) and pregnancy outcomes. Some of these have reported increased risks for cardiac anomalies, with OR ranging from 3.4 (95% CI 1.6–6.9) to 6 (95% CI 1.7–21.3) *(122,123)*. But it is not possible to reach any conclusion with respect to the precise role of TCE. Pregnancy outcomes have been studied in several cohorts in the general population exposed via the oral route (drinking-water) in the United States. Developmental abnormalities (cardiac, neural tubes, cleft palate, eye and ear malformations), perinatal deaths and low birth weights were observed *(42,87,124–128)* but the presence of possible bias or misclassification precludes confident conclusions being made. An interaction between maternal age and TCE exposure in increasing congenital heart defects has been observed by Yauck et al. *(129)*, although the mechanism by which this might occur is unknown. Finally, the National Research Council suggested that epidemiological observations concerning malformations (particularly cardiac ones) and delayed intrauterine growth in humans exposed to TCE are consistent with the animal studies and are supported by mechanistic studies and a relative agreement in the type of malformations.

However, to date, no definitive conclusion has been put forward for humans and it is not possible to extract from these studies either a well-defined dose–response relationship or a LOAEL for assessing the risk of TCE, particularly since the populations are often concomitantly exposed to several toxic substances (halogenated solvents, metals, etc.) *(87)*.

Carcinogenic effects

The results of the Finnish cohort study, in which 2050 men and 1924 women were exposed to TCE and other solvents in the context of their work *(130)*, demonstrated a statistically significant increase in non-Hodgkin's lymphoma and cervical cancer, with a significantly higher risk in the individuals with the highest urinary trichloroacetic acid concentrations (signal-to-interference ratio 4.4; 95% CI 1.4–10.1), and an increase in liver cancers for workers exposed for more than 20 years (RR = 6.1, 95% CI 2.8–17.7). Kidney cancers were not significantly increased. However, the exact exposure duration was not known and the workers were exposed to other solvents (although the estimates were adjusted to the

urinary trichloroacetic acid concentrations). In the same cohort, the risk of liver cancer was increased among male printers, lacquerers and varnishers exposed to chlorinated hydrocarbons (RR = 2.65, 95% CI 1.38–5.11). The authors suggest a role of TCE, which is consistent with previous data *(131)*.

The results of the Swedish cohort study, in which 1670 workers (1421 men and 249 women) were exposed to TCE *(132)*, demonstrated that mortality and morbidity from cancer were not significantly higher in these exposed individuals than in the general population. The majority of workers had urinary trichloroacetic acid levels below 50 mg/l, which may correspond – according to the authors – to an exposure of approximately 20 ppm.

A study conducted on a cohort of 14 457 American aircraft maintenance workers exposed to multiple solvents, including TCE, demonstrated a non-significant increase in mortality due to liver cancer, kidney cancer and non-Hodgkin's lymphoma: a statistically significant increase was observed for multiple myelomas (SMR 236; 95% CI 87–514) and non-Hodgkin's lymphoma (SMR 212; 95% CI 102–390) in white women, and for cancers of the bile duct and liver in white men who died after 1980 (SMR 358; 95% CI 116–836). Exposures were classified according to certain indices (as a function of occupational category) and did not therefore permit a quantitative approach. When only individuals exposed to TCE were examined (6929 people), no significant association was found between the additional risk of cancer and TCE measurements *(133)*.

A recent case-control study in Germany analysed the relationship between exposure to organic solvents (including TCE) and malignant lymphoma in 710 patients. A statistically significant association was found between high exposure to chlorinated solvents and malignant lymphoma (OR 2.1; 95% CI 1.1–4.3). When TCE only is considered, this trend persists (borderline statistical significance) *(134)*.

Other studies conducted in general populations exposed to TCE via drinking-water have demonstrated associations between (increased) incidence of leukaemia or non-Hodgkin's lymphoma and TCE exposures, which is consistent with the data from occupational cohorts. Scott & Chiu *(135)* reviewed recently published scientific literature examining cancer and TCE exposure and suggested that the studies appear to provide further support for the kidney, liver and lymphatic system as targets of TCE toxicity.

All the retrospective cohort studies conducted on TCE have methodological limitations linked either to the absence of quantification of exposures to TCE, to potential co-exposures not taken into account in occupational environments, or to the low number of subjects studied. Nevertheless, some epidemiological studies have measured trichloroacetic acid in urine, which can be directly related to TCE exposure *(130)*. The strongest associations between TCE exposure and human cancer are for the kidney, liver and lympho-haematopoietic system, sites where TCE causes cancer in rats and mice *(102)*. These aspects of biological

plausibility and coherence suggest that a cause-and-effect association between TCE exposure and cancer in humans is credible, even if the interpretation of individual studies may be difficult.

However, several recent meta-analyses have been conducted that did not confirm previous findings. A meta-analysis of 14 occupational cohort and four case-control studies of workers exposed to TCE investigated the relationship between TCE exposure and risk of non-Hodgkin's lymphoma. The comparisons carried out by the authors did not indicate exposure–response trends, suggesting insufficient evidence of a causal link between TCE exposure and non-Hodgkin's lymphoma *(136,137)*. Alexander et al. *(138)* found the same results in analysing occupational studies of TCE exposure and liver/biliary tract cancer. The main conclusions drawn are that exposure to solvents may cause cancer in humans and that TCE is likely to be one of these, but a number of challenging issues need to be considered before concluding clear causal relationships between TCE exposure and cancer *(139)*.

Thus, considering the bias and confounding in epidemiological studies, human evidence of the carcinogenicity of TCE can be considered limited. IARC has classified TCE as probably carcinogenic to humans (Group 2A) based on sufficient evidence in animals and limited evidence in humans *(3)*.

Based on data presented by the USEPA in its health risk assessment of TCE *(102)*, and particularly the cancer potency values, Lewandowski & Rhomberg *(140)* proposed a method for selecting the most appropriate carcinogenic inhalation unit risk estimate for TCE. The method is based on an in-depth analysis of the key studies used to derive unit risks in both animals and humans (protocol, rigour, statistical power, characterization of exposure, confusion factors, critical effects, etc.). The authors evaluated the validity of the studies (suitability of the protocol and dose–response relationships for a quantitative assessment) and the plausibility of the effects (with the use of Hill's criteria). These considerations led to the choice of the unit risk derived from the Finnish cohort study, based on the increase in the incidence of hepatic tumours. The selected unit risk was 9×10^{-7} per $\mu g/m^3$.

Sensitive populations

An extensive review of factors that may affect risk of exposure to TCE, with a particular examination of age (children), genetics, sex, altered health state, co-exposure to alcohol and enzyme induction, was published in 2000 *(141)*.

Since the metabolism of TCE is largely implicated in its toxic mechanisms of action, all the known polymorphisms, and particularly those concerning the CYP2E1, glutathione-S-transferase (GST) and N-acetyltransferase enzymes, are liable to modify individual sensitivity to this substance, although it is currently impossible to accurately quantify the scale of this modification or the number of people affected by these polymorphisms. In the example of polymorphism

of GST, it appears that some subgroups of the population have a risk of kidney cancer that is four times higher than others *(102)*. However, a recent study of about 134 renal cell cancer cases from Brüning et al. *(142)* does not confirm the hypothesis of an influence of the deletion polymorphisms of GST on renal cell cancer development due to exposure to TCE *(143)*. With respect to the polymorphism of CYP450 2E1, Pastino et al. *(141)* reported that a 10- to 50-fold variability in the protein or its activity has been observed in humans.

Merdink et al. *(45)* showed that individuals with an impaired capacity for glucuronidation may be very sensitive to the CNS-depressant effects of high doses of chloral hydrate, which are commonly attributed to plasma levels of TCE.

Individuals with hepatic and/or renal failure may constitute a more sensitive population owing to reduced metabolism of TCE and/or a reduction in the elimination of its toxic metabolites, whether these disturbances be genetic, environmental (alcohol, medicinal products, etc.) or secondary to a disease. Individuals with a history of cardiac arrhythmias may be more susceptible to high-level TCE exposure *(2)*. The provisional version of the 2001 assessment made by the USEPA also cites diabetics among sensitive populations owing to their specific susceptibility to neuropathies and certain cancers, and the specific effects of TCE on the metabolism of carbohydrates and cell signalling *(102)*.

Finally, according to ATSDR *(2)*, people with a high consumption of alcohol or taking disulfiram may be more sensitive to the neurological effects of TCE, owing to an interaction process.

Health risk evaluation

Critical health outcomes

TCE is a chlorinated solvent. Its main health effects are neurotoxic and carcinogenic. Immunotoxic, hepatic and developmental effects are also reported.

Neurotoxic effects

Effects on the CNS (damage affecting the optic and trigeminal nerves) have been observed in humans and animals exposed to high acute (600–1000 mg/m^3) or moderate chronic (38–87 mg/m^3) occupational levels. Sufficient evidence exists to conclude that there is an association between TCE and neurotoxic effects.

Immunotoxic effects

The evidence is suggestive for an association between TCE exposure and the exacerbation or induction of autoimmunity. Several mechanistic hypotheses are suggested in rodents but further research is needed before firm conclusions can be reached. Recent studies in humans confirm the possibility of immune disorders in individuals exposed occupationally to high-to-moderate levels of TCE (18–683 mg/m^3). However, not enough human studies are available to allow a conclusion to be drawn on causality, especially because the human immune re-

sponse varies greatly among individuals. It is concluded that there is limited evidence of an association between immunological effects and TCE exposure.

Hepatic effects

Transient hepatic hypertrophy has been observed in rodents, but the results of studies are equivocal. The human epidemiological studies suffer from methodological limitations, particularly in terms of characterization of exposure. In addition, individuals exposed to TCE were often also exposed to other solvents. It is concluded that there is limited evidence of an association between hepatic effects and TCE exposure.

Developmental effects

Developmental effects, notably cardiac and eye malformations, have been reported in rodents but the results are inconsistent (possible maternal toxicity, positive results only in oral studies in rats). Occupational studies in humans suggest a link between the use of degreasing solvents and adverse pregnancy outcomes. Epidemiological studies in the general population suggest malformations, perinatal death and low birth weight, but possible bias and exposure misclassification prevent firm conclusions being drawn. There is thus insufficient evidence for an association between developmental effects and TCE exposure.

Carcinogenic effects

Animal evidence is sufficient to demonstrate carcinogenic effects of TCE by both oral and inhalation routes, and there is sufficient evidence to conclude that TCE is at least weakly genotoxic. Positive associations have been established between occupational exposure and risks for cancer of the liver, kidney and bile duct and non-Hodgkin's lymphoma. Lung and testis tumours observed in rodents have not been reported in humans but cannot be excluded. The presence of possible exposure misclassification or co-exposure in occupational cohort studies somewhat weakens the confidence in the association. Overall, it is concluded that sufficient evidence exists to suggest an association between TCE exposure and cancer (liver and kidney).

Health relevance of indoor exposures

Since there is sufficient evidence that TCE is a genotoxic carcinogen, all exposures indoors are considered relevant and no threshold can be determined.

Inhalation of TCE is the main route of exposure in the general population. Ambient and indoor air concentrations of TCE are generally less than 1 $\mu g/m^3$ in European and North American countries. Indoor TCE levels of up to 30 $\mu g/m^3$ (90th percentile) have been reported during the EXPOLIS study (1998–1999). More recent studies in French dwellings and American office buildings showed lower levels (95th percentile 7.4 and 2.6 $\mu g/m^3$, respectively).

Consumers may be exposed to TCE by using wood stains, varnishes, finishes, lubricants, adhesives, typewriter correction fluid, paint removers and certain cleaners, where TCE is used as a solvent. Contaminated water or soil may also contribute to indoor pollution through TCE.

Conclusions of other reviews

The previous WHO air quality guideline *(37)* was based on the unit risk estimate of 4.3×10^{-7} $(\mu g/m^3)^{-1}$ derived from the increase of Leydig cell tumours in rats.

IARC has considered TCE a probable carcinogen since 1995 (Group 2A, limited evidence in humans but sufficient in animals). The EU classified it as carcinogenic category 2, risk phrase R45 (may cause cancer) in 2001 for the same reasons. The IARC evaluation is based on experimental data and on three human cohort studies conducted in Finland, Sweden and the United Kingdom, which demonstrated an increased risk of several cancers including liver, kidney and bile duct cancers and non-Hodgkin's lymphoma *(3)*. An additional risk for cervical cancer was observed in two of the studies.

Guidelines

The existence of both positive and negative results has in the past led risk assessors to different interpretations of TCE toxicity and to divergent estimates of human cancer risk *(144,145)*. For a health risk evaluation, bearing in mind recent data on a mechanism of action that is not species-specific, the evidence for weak genotoxicity, and the consistency between certain cancers observed in animals and in humans (in particular liver cancer), it is prudent to consider that the carcinogenicity in animals, the positive epidemiological studies and the plausibility of a human cancer risk leads to the recommendation of a non-threshold approach with a risk estimate rather than a safe level.

Therefore, carcinogenicity (with the assumption of genotoxicity) is selected as the end-point for setting the guideline value. The unit risk estimate of 4.3×10^{-7} $(\mu g/m^3)^{-1}$, derived on the basis of increased Leydig cell tumours (testicular tumours) in rats, is proposed as the indoor air quality guideline. This was also the conclusion of WHO in 2000 *(37)*, the EU in 2004 *(1)* and the French Agency for Environmental and Occupational Health in 2009 *(42)*.

The concentrations of airborne TCE associated with an excess lifetime cancer risk of 1:10 000, 1:100 000 and 1:1 000 000 are respectively 230, 23 and 2.3 $\mu g/m^3$.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

Summary of main evidence and decision-making in guideline formulation

Critical outcome for guideline definition

Carcinogenicity (liver, kidney, bile duct and non-Hodgkin's lymphoma), with the assumption of genotoxicity.

Source of exposure–effect evidence

Increased Leydig cell tumours (testicular tumours) in rats provided the basis for calculation of unit risk, applying a linearized multistage model *(37)*.

Supporting evidence

- Sufficient evidence exists for an association between TCE exposure and cancer (liver and kidney) *(3)*.
- Unit risk derived from a cohort study of occupationally exposed adults *(139)*, based on the increase in the incidence of hepatic tumours, was 9×10^{-7} per $\mu g/m^3$ *(140)*.

Results of other reviews

- IARC: Group 2A (limited evidence in humans but sufficient in animals) *(3)*.
- EU: carcinogenic category 2, risk phrase R45 (may cause cancer) *(1)*.

Guidelines

- Unit risk estimate of 4.3×10^{-7} per $\mu g/m^3$.
- The concentrations of airborne TCE associated with an excess lifetime cancer risk of 1:10 000, 1:100 000 and 1:1 000 000 are respectively 230, 23 and 2.3 $\mu g/m^3$.

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9. Tetrachloroethylene

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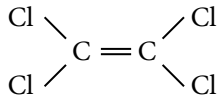
General description

Tetrachloroethylene (PCE) (CAS Registry Number 127-18-4; C_2Cl_4; molecular weight 165.83) is a readily volatile, colourless liquid with an ether-like smell *(1)*. Its main physical and chemical properties are as follows *(2–5)*: molecular weight 165.83 g/mol; density (at 20 °C) 1.6227 g/ml; melting point approximately –22 °C; boiling point 121 °C; water solubility (at 25 °C) 150 mg/litre; vapour pressure 18.47 mmHg at 25 °C *(2)*, 1.9 kPa at 20 °C, 3.2 kPa at 30 °C and 6.0 kPa at 40 °C *(3)*; Henry's Law constant 0.018 atm-m^3/mol at 25 °C; log K_{ow} (octanol/water partition coefficient) 3.40 (measurement value) and 2.97 (estimated value); and log K_{oc} (octanol/carbon partition coefficient) 177~350 (measurement value). The reaction rate constant against the hydroxyl radical is 1.7×10^{-13} cm^3/molecule per second at 25 °C, against ozone 2.0×10^{-23} cm^3/molecule per second at 25 °C and against the NO_3 radical 5.2×10^{-17} cm^3/molecule per second.

Its structural formula is:



Common synonyms include perchloroethylene, PCE, ethylene tetrachloride, tetrachloroethene, 1,1,2,2-tetrachloroethylene, carbon dichloride, perchlor, tetrachloroethane, carbon bichloride, PERC, PCE and perk.

Conversion factors

At 760 mmHg and 20 °C, 1 ppm = 6.897 mg/m^3 and 1 mg/m^3 = 0.145 ppm; at 25 °C, 1 ppm = 6.782 mg/m^3 and 1 mg/m^3 = 0.147 ppm.

Applications and uses

Major industrial applications of PCE are as a synthetic raw material of hydrochlorofluorocarbon, a dry cleaning agent, a degreaser for manufactured metal parts and an industrial solvent. Other applications include the finishing and processing of textiles, the production of paint removers and printing inks, and the formulation of adhesives and specialized cleaning fluids. Consumer products

that may contain PCE include adhesives, fragrances, spot removers, stain removers, fabric finishes, water repellents, wood cleaners, motor vehicle cleaners and dry-cleaned fabrics *(6–8)*. In Japan, 69%, 18%, 12%, and 1.3% of PCE was used as a synthetic raw material of hydrochlorofluorocarbon, a dry cleaning agent, a degreaser and an industrial solvent, respectively *(9)*.

Production

The estimated production volume in the United States in 1990 was 137 kilotonnes, compared to 282 kilotonnes in 1980 *(2)*. In 1994, the total production of PCE in the EU was 164 kilotonnes. Of this amount, 78 kilotonnes was sold for use within the EU, 56 kilotonnes were exported and the remainder used as a chemical intermediate within the chemical industry *(10)*. For Japan and the United States, it was 178 and 102 kilotonnes, respectively *(1)*. In Canada, where PCE is no longer produced, the demand in 1990 was estimated at 14 kilotonnes *(7)*. In Japan, the production and supply of PCE was 25 and 37 kilotonnes, respectively. No estimates of consumption levels are available for other parts of the world.

Analytical methods in air

Common methods of measuring indoor concentrations of TCE include integrated active and passive sampling methods using tubes packed with a carbon-based sorbent or evacuated SUMMA canisters (passivated canister sampling apparatus), or diffusion samplers such as charcoal badges. Canister sampling involves controlling the flow of air into a pre-evacuated canister. Sorbent tubes and badges retain compounds according to the affinity of the sorbent for that compound. For sorbent or charcoal sampling, the analytes must first be extracted thermally or chemically, then separated using gas chromatography and identified using a detection method such as mass spectrometry *(11)*. Personal exposure studies often use these sorbent-based methods.

Environmental fate

There are no known natural sources of PCE. The Henry's Law constant indicates that PCE is expected to volatilize rapidly from water surfaces and that volatilization from moist soil surfaces may occur *(1)*. Concentrations in ambient air may fluctuate widely over relatively short periods of time depending on the strength of the emission source, variations in wind direction and velocity, and scavenging and photodecomposition *(6)*.

The half-life in the atmosphere has been estimated to range from 70 to 250 days *(2)*.Considering the atmospheric concentrations and reaction rate constant of the hydroxyl radical and ozone, this removal from atmosphere is mostly due to reaction with hydroxyl radicals. This process is temperature-dependent, with increased reaction rates in the summer. The results of biodegradability tests sug-

gested that the biodegradability of PCE is extremely low in environmental water *(12,13)*; it may persist in groundwater for several months or more *(7)*.

The main sources resulting in ambient air concentrations are industrial emissions and releases from building and consumer products. Releases are primarily to the atmosphere, but the compound is also released to surface water and land in sewage sludges and in other liquid and solid waste, where it can evaporate rapidly to the atmosphere.

ATSDR has estimated that 80–85% of the PCE used annually in the United States is released into the atmosphere *(2)*. Atmospheric emissions result from evaporation during dry cleaning, metal degreasing, the production of fluorocarbons and other chemicals, and miscellaneous solvent-associated applications *(14)*. However, the percentage is likely to be lower in the United States at present, owing to improved technology and regulatory restrictions. Almost all PCE enters the atmosphere unchanged. A small proportion enters water and wastewater. From surface water, PCE volatilizes owing to its relatively low water solubility and high vapour pressure.

Indoor sources and pathways of exposure

Inhalation is the most common route of exposure to PCE for the general population. Ingestion of contaminated drinking-water may also be important in areas with highly contaminated water. While PCE has been found in some food items, particularly from local source contamination, not enough data are available to estimate exposure through this route *(2)*.

Indoor sources

Consumer products described above are sources of indoor PCE exposure. Contaminated drinking-water may be a source of indoor PCE exposure when taking a shower or washing dishes. Workers from dry cleaning establishments have been found to become sources of PCE at home by exhaling PCE in their breath *(15)*. Dry-cleaned clothes are also possible sources of PCE in a house.

The air in dry cleaning facilities and neighbouring homes or facilities can contain elevated concentrations of PCE. Soil pollution with PCE has resulted in indoor air concentrations of these chemicals in residential homes. These chemicals can evaporate from the soil, permeate through floors and result in elevated indoor air concentrations. PCE can permeate through synthetic water pipes and contaminate drinking-water, thus leading to exposure during bathing or showering.

Drinking-water

Exposure can take place by drinking contaminated water as well as volatilization. In the United States, PCE is not detectable in drinking-water in most cases. The EPA Groundwater Supply Survey of 945 drinking-water systems nationwide reported PCE in 75 out of 945 systems in 1984; the median level of the positive

samples was about 0.75 μg/litre, with a maximum of 69 μg/litre *(2)*. In several studies in Canada, PCE was detectable in 6–60% of the tested samples. Reported mean values ranged from 0.1 to 0.9 μg/litre *(6)*. In several other countries, including Germany and the United Kingdom, similar results have been observed *(8,16)*. In some villages in Finland, concentrations of up to 180 μg/litre were found *(17)*. In Japan, PCE levels in 99.7% of drinking-water (n = 5600) were less than 1 μg/litre with a maximum of 7 μg/litre in 2007 *(18)*.

Food

Data on concentrations of PCE in food are scarce. In some studies from Germany and Switzerland reported in the early 1980s, relatively high total intakes of 87–170 μg/day were found *(16)*. The results of market basket surveys in the United States, reported in 1987 and 1988, indicated lower levels. From the results of these surveys, total daily intake via food has been estimated at 0.12–65 μg/kg body weight *(6)*. Several groups of researchers have reported elevated concentrations of PCE in fatty food products in residences and markets, owing to contamination from dry cleaning establishments nearby. In a supermarket near a dry cleaning shop in Germany, concentrations were 36 μg/kg and 110 μg/kg in cheese and margarine, respectively *(8)*. In one instance in the United States, a very high PCE concentration was found in margarine (up to 50 mg/kg) in a shop next door to a dry cleaning establishment *(2)*. Moreover, food grown on contaminated soil can contain PCE. In Japan, the daily maximum levels of PCE in the diet between 1990 and 1999 (n = 72~81 in each year) were 4.4 μg/kg wet weight *(14)*.

Indoor air concentrations and relationship with outdoor levels

Residential concentrations

In several United States cities (New York, Los Angeles, Chicago, Minneapolis, St Paul, Baltimore, Elizabeth and Houston), median indoor residential concentrations ranged from 0.4 μg/m^3 in spring (Minneapolis) to 3.5 μg/m^3 during winter (New York City) *(19–26)*. The 90th percentiles ranged from 1 μg/m^3 in Minneapolis in the spring to 14 μg/m^3 in New York City during the summer *(23)*.

Geometric mean concentrations of PCE in the homes of dry cleaning workers have been found to be 265 μg/m^3, while non-exposed homes had a mean concentration of 2 μg/m^3 *(15)*. Also, shops, offices or homes that share a building with a dry cleaning establishment have been found to have higher levels of PCE than those that are not near dry cleaners. A study of apartments in neighbourhoods with different income levels and ethnic compositions in New York City between 2001 and 2003 found overall geometric mean levels of 34 μg/m^3, although in low-income neighbourhoods, the geometric mean was 256 μg/m^3. Apartments with no dry cleaners in the building had a geometric mean concentration of 3 μg/m^3. Before 1997, when New York adopted stricter regulations for dry cleaners, PCE

was found to be about 340–360 μg/m^3 in residential buildings with a dry cleaning establishment *(27)*.

In a national survey of dwellings in France, a median concentration of 1.4 μg/m^3 was found, with a 90th percentile of 5.2 μg/m^3 *(28)*. In the European multinational urban air study EXPOLIS *(29)*, median levels of PCE inside homes in Helsinki were not detectable, while they were 0.6 μg/m^3 in Basel. The 90th percentile in Basel was 2.9 μg/m^3. In Oxford, United Kingdom, the median indoor residential PCE concentration was 1.9 μg/m^3, and 6.3 μg/m^3 at the 90th percentile. Homes in Athens had a median indoor level of 4 μg/m^3 and a 90th percentile level of 14.3 μg/m^3. Milan and Prague were found to have median concentrations of 7.4 and 8.7 μg/m^3, respectively, with 90th percentiles of 28.1 μg/m^3 and 26.1 μg/m^3, respectively. Median outdoor residential PCE levels were under the detection limit in Helsinki, 0.7 μg/m^3 in Basel and 1.7 μg/m^3 in Oxford. The 90th percentiles in Basel and Oxford were 1.4 μg/m^3 and 3.4 μg/m^3, respectively. In Athens, Milan and Prague, the median outdoor residential levels were 2.3 μg/m^3, 4.1 μg/m^3 and 5.3 μg/m^3, respectively. Median personal exposure levels were lower than the indoor levels.

In 25 homes surveyed in Shimizu, Japan, geometric mean indoor PCE concentrations were 0.16 μg/m^3 in summer and winter, with geometric standard deviations of 2.34 μg/m^3 in summer and 2.77 μg/m^3 in winter *(30)*. The geometric mean concentration outside these homes was 0.11 μg/m^3 in both summer and winter, with geometric standard deviations of approximately 2 μg/m^3 in both seasons. In a national survey of dwellings in Japan, median indoor PCE concentrations in residential houses in 1997 (n = 180) and 1998 (n = 205) were 0.4 μg/m^3 (mean 1.8 μg/m^3; maximum 83.5 μg/m^3) and 0.3 μg/m^3 (mean 1.9 μg/m^3; maximum 43.4 μg/m^3), respectively *(31)*.

Non-residential microenvironments

Predicted PCE concentrations in the air around metal degreasing machines were found to range from about 10 000 μg/m^3 to above 1 million μg/m^3, depending on the type of machine. In Germany, mean personal air samples in occupational environments with degreasers ranged from 18 000 to 40 000 μg/m^3 *(10)*.

Exposure to PCE from dry cleaning affects both workers and members of the general public. A study in Finland of personal exposure of workers in commercial and industrial dry cleaning operations using dry-to-dry machines found that machine operators had the highest exposure levels (28 000 and 32 000 μg/m^3 at commercial and industrial sites, respectively). Customer service workers had the lowest exposures, with an average of about 800 μg/m^3 *(32)*. Another study of dry cleaning establishments in Chicago found indoor levels of PCE ranging from 12 000 to 355 000 μg/m^3 *(33)*.

A survey of stores in a one-level commercial building in New Jersey found a median concentration of 690 μg/m^3 and a 90th percentile of 4200 μg/m^3 in a

dry cleaning establishment in the building, and a median of 570 μg/m^3 and 90th percentile of 5800 μg/m^3 (8 hour average) in a neighbouring clothes rental shop, which may have also contained dry-cleaned clothes *(34)*. The neighbouring shop on the other side had lower levels, but the median was still nearly 90 μg/m^3, a level much higher than the average indoor environment. Dry cleaned clothes have been shown to emit PCE *(2,32)*.

A survey of 70 office buildings across the United States (in which there were no complaints) found a median indoor PCE level of 1.5 μg/m^3 and a 95th percentile of 18 μg/m^3 *(35)*. A study of mechanically ventilated non-office and office buildings in Hong Kong SAR, China found arithmetic mean levels of 1.4 μg/m^3 (SD = 3.4) and 1.9 μg/m^3 (SD = 9.2), respectively *(36)*. Median indoor concentrations at workplaces of the EXPOLIS participants were under the detection limit in Helsinki, 1.2 μg/m^3 in Basel, 3.5 μg/m^3 in Athens, 5.4 μg/m^3 in Milan and 3.7 μg/m^3 in Prague. The 90th percentile of workplace levels were 3.1 μg/m^3 in Basel, 10.6 μg/m^3 in Athens, 17.5 μg/m^3 in Milan and 10 μg/m^3 in Prague. The workplaces were typically offices. A survey of stores in Boston, MA found that geometric mean levels of PCE in stores and restaurants were near or under 3 μg/m^3 *(37)*.

Ambient air

Residential outdoor median concentrations ranged from 0.3 μg/m^3 in Minneapolis (spring) to 1.7 μg/m^3 in Los Angeles (winter). The median outdoor concentrations of PCE in Shimizu (Japan) were 0.2 μg/m^3 (mean 0.5 μg/m^3; maximum 4.7 μg/m^3) and 0.2 μg/m^3 (mean 0.7 μg/m^3; maximum 10.8 μg/m^3), respectively *(30)*. Outdoor levels in rural Canada were found to have a mean of 0.04 μg/m^3 and a maximum of 7 μg/m^3 *(38)*.

Indoor : outdoor ratios in New York and Los Angeles from a study in a low-income group of teenagers were between 1 and 2 at the median and did not have large standard deviations relative to the median (except for New York homes in the winter) *(23)*. The earlier Total Exposure Assessment Methodology (TEAM) study found higher indoor : outdoor ratios in the cities of Bayonne and Elizabeth, NJ, with arithmetic means ranging from 2 in summer to 7 in winter and 5 in the winter in Los Angeles *(39,40)*. The medians were not reported but are likely to have been lower than the arithmetic means.

Personal exposure

Median personal exposures of the teenagers were 2.2 μg/m^3 in Los Angeles and 3.7 μg/m^3 in New York, although the mean in New York was 8.8 μg/m^3, indicating a more skewed distribution with some higher values *(19–26)*. The New York indoor home distribution was also fairly skewed. The RIOPA study in Los Angeles, Elizabeth and Houston found that adult personal air concentrations had lower medians than means, with a particularly large difference in Elizabeth,

where the median was 0.56 μg/m^3 and the mean was 17.3 μg/m^3 *(26)*. Indoor and outdoor residential mean concentrations in Elizabeth, however, were near 1 μg/m^3 and were detectable in only 24% of outdoor samples and 39% of indoor samples, while in personal samples PCE was detected in 44% of the samples *(26)*.

Personal exposures to PCE are most influenced by indoor concentrations. PCE can reach extremely high levels indoors, even in non-occupational environments such as homes or businesses that are in the same building as or close to dry cleaners. The TEAM studies found that higher personal PCE exposures were associated with visits to dry cleaners *(39,40)*. Unlike other industries that use PCE, such as metal degreasing, dry cleaners are often located in residential, non-industrial commercial and business districts and may affect both the occupants of neighbouring establishments and food. Indoor environments next to dry cleaners have been found to have PCE concentrations of several hundreds of μg/m^3. Indoor environments without sources of PCE have concentrations well below 10 μg/m^3, with median concentrations near 1 μg/m^3 in many areas. Dry-cleaned items can be an occasional source of PCE in some homes.

Toxicokinetics

Absorption

PCE is readily absorbed in the gastrointestinal tract and the lungs. Pulmonary uptake is proportional to ventilation rate, duration of exposure and, at lower atmospheric concentrations, the concentration in the inspired air *(2)*. In both humans and animals, initial uptake following inhalation is rapid, with rates levelling off after a few hours of exposure. The available data suggest that a high proportion is absorbed in humans, but actual percentages have not been reported. In rats, the proportion absorbed was approximately 55–70% after 1 minute, gradually declining to 40–50% after 2 hours *(41)*.

Dermal absorption from the gaseous phase is negligible. However, dermal absorption of significant amounts of PCE is probably possible in some situations. Dermal absorption of PCE solutions resulted in measurable levels of the compound in the breath, reaching a maximum 10 minutes after exposure *(16)*. Experiments in hairless guinea-pigs have shown substantial dermal absorption from dilute aqueous solutions *(21)*. In vitro dermal absorption of PCE in aqueous solution through freshly prepared and previously frozen human skin was measured and compared to absorption of other volatile organic compounds in aqueous solution *(42)*. The dermal absorption of PCE from a soil matrix was compared in rats and humans using real-time mass spectrometric exhaled breath technology and physiologically based pharmacokinetic (PBPK) modelling *(43)*.

Distribution

Repeated inhalation exposure to PCE results in accumulation of the compound in the body, especially in fatty tissue since it is lipid-soluble. PCE crosses the

placenta and can be found in breast milk; the fetus and nursing neonates may therefore be at increased risk of adverse effects from maternal exposure *(2,44,45)*. In rats, distribution to the brain, liver and kidneys has also been demonstrated *(2,46)*. In a study in mice, transplacental transport of unchanged PCE has been observed *(2)*. In rats and goats, it has been shown that excretion of unchanged PCE in milk occurs after intraruminal administration *(23,24)*. Following inhalation exposure of lactating rats to a concentration of 4070 mg/m^3 (600 ppm) for 2 hours, total body burden for the pups was up to about 14 mg/kg body weight *(23)*. Since women have a higher proportion of body fat than men, it is assumed that women retain PCE longer *(47)*.

Biotransformation

In experiments in humans and rats, it was observed that most of the absorbed amount of PCE is exhaled unchanged. The two principal pathways of PCE metabolism that occur in the liver and kidney of experimental animals are cytochrome P450-dependent oxidation and glutathione conjugation. The hepatotoxic, nephrotoxic and carcinogenic effects of PCE depend on its metabolism to reactive metabolites, which may covalently bind to cellular macromolecules.

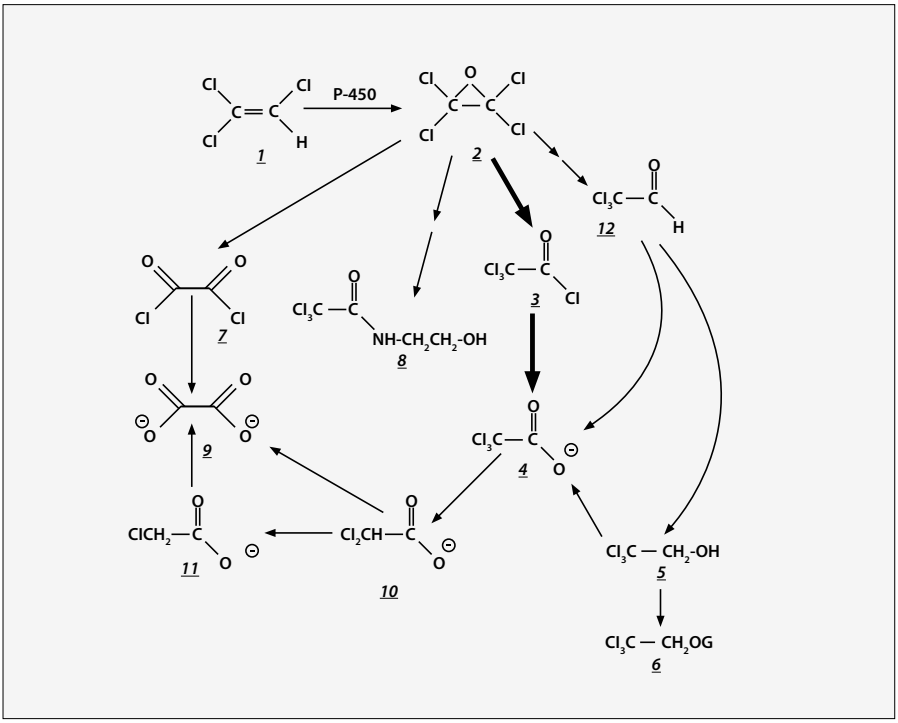
Cytochrome P450 enzymes primarily catalyse PCE oxidation. Presumably, CYP2E1 plays an important role in this process in rodent liver and kidney as well as human liver. This results in the formation of a PCE-epoxide, which further reacts to trichloroacetyl chloride. Trichloroacetyl chloride can react with amino groups in macromolecules, resulting in hepatotoxicity. When it reacts with water it forms trichloroacetic acid.

Trichloroacetic acid is the principal metabolite recovered from urine in both humans and rodents following inhalation exposure to PCE. Another metabolite that can be formed by the cytochrome P450 pathway is dichloroacetate. Di- and trichloroacetate are associated with hepatic toxicity and carcinogenicity. Other metabolites of PCE by the P450 pathway that have been identified are shown schematically in Fig. 9.1 *(48,49)*.

There is a broad range of halogenated hydrocarbons and other small organic molecules that are oxidized by CYP2E1. Several drugs as well as physiological or pathological conditions may lead to the induction of CYP2E1. This implies that under certain conditions, prior or concurrent exposure to chemicals such as ethanol or acetaminophen may influence the response to PCE. Also, individual susceptibility due to genetic polymorphisms in CYP450-dependent metabolism can result in altered toxicity.

PCE is conjugated by glutathione to S-(1,2,2-trichlorovinyl)glutathione (TCVG). No significant effects were found of PCE or TCVG on cytotoxicity or mitochondrial function in isolated hepatocytes from rats or in isolated liver mitochondria from rats or mice. Therefore, it is unlikely that the liver is a major acute target for PCE or TCVG. Glutathione conjugation of PCE, followed by ac-

Fig. 9.1. Metabolism of PCE by the P450 pathway



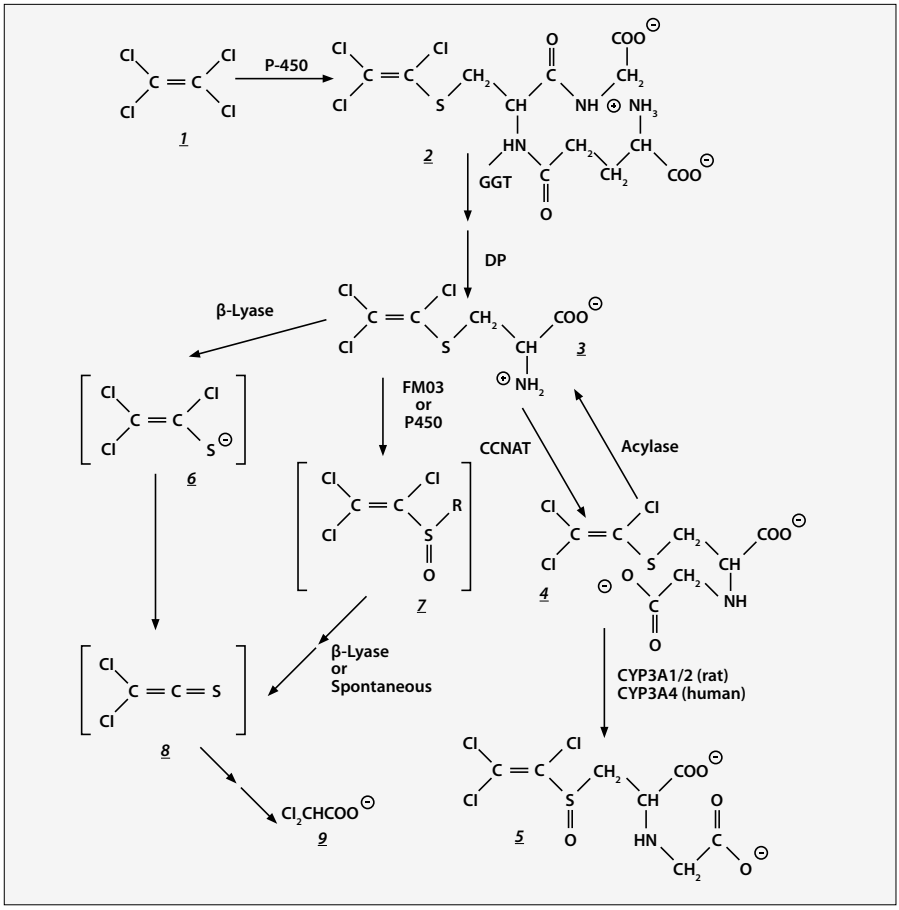
Note. Identified urinary metabolites: 1 = PCE; 2 = PCE epoxide; 3 = trichloroacetyl chloride; 4 = trichloroacetate; 5 = trichloroethanol; 6 = trichloroethanol glucuronide; 7 = oxalate dichloride; 8 = trichloroacetyl aminoethanol; 9 = oxalate; 10 = dichloroacetate; 11 = monochloroacetate; 12 = trichloroacetaldehyde.
Source: Lash & Parker *(48)*.

tivation of trichlorovinylcysteine (TCVC), is responsible for nephrotoxicity and possibly nephrocarcinogenicity *(49,50)*. Fig. 9.2 shows the metabolites of PCE by the glutathione conjugation pathway, so far as they have been identified to date.

Species-dependent differences in biotransformation

Mice metabolize PCE to trichloroacetic acid to a greater extent than rats. In rats, saturation of the oxidative metabolism at exposure concentrations exceeding 678 mg/m^3 (100 ppm) prevents the occurrence of the high trichloroacetic acid concentrations that are observed in mice at these dose levels. The available evidence indicates that in humans too, saturation of the oxidative metabolism of PCE occurs at ≥ 678 mg/m^3 (≥ 100 ppm) *(51)*. In a comparative study, the urinary levels of *N*-acetyl-*S*-(1,2,2-trichlorovinyl)-*L*-cysteine, one of the final metabolites in the glutathione biotransformation pathway, were shown to be higher in rats than in mice after inhalation exposure to PCE. In vitro tests in hepatocytes and kidney fractions of rats, mice and humans suggest that the potential for this biotransformation in the kidneys is also lower in humans than in rats *(2,6,52)*. Experimental data show that rates of TCVG formation in rats and mice

Fig. 9.2. Metabolism of PCE by the glutathione conjugation pathway



Note. Identified urinary metabolites: 1 = PCE; 2 = TCVG; 3 = TCVC; 4 = NAcTCVC; 5 = NAcTCVC sulfoxide; 6 = 1,2,2-trichlorovinylthiol; 7 = TCVCSO; 8 = 2,2-dichlorothioketene; 9 = dichloroacetate. Enzymes: GST, GGT, dipeptidase (DP), ß-lyase, FMO3, CCNAT, CYP3A1/2 and CYP3A4. Unstable, reactive metabolites are shown in brackets.

Source: Lash & Parker *(48)*.

are higher in males than in females, the formation rates in mice being higher than in rats *(48,53)*.

The overall kinetics of PCE oxidative metabolism differs significantly between humans and rodents. The excretion of trichloroacetic acid after inhalation of PCE has been shown to be slower in humans than in rats. The elimination half-time of trichloroacetic acid in the urine was approximately 4.1-fold longer in humans than in rats exposed to 10 or 40 ppm PCE. Maximal trichloroacetic acid concentrations in blood were 3- to 10-fold lower (depending on dose) in humans than in rats *(48,54)*. It is assumed that saturation of PCE metabolism occurs at lower doses in humans *(55,56)*.

While the target organs for toxicity in general are similar for different species, this is not the case for carcinogenicity.

Sex-dependent differences in biotransformation

Regarding renal toxicity, sex differences have been found in experiments on rats and mice. PCE is demonstrated to cause a significant release of lactate dehydrogenase in isolated kidney cells from male but not from female rats. TCVG causes much more lactate dehydrogenase to be released from male than from female rat kidney cells. Examination of effects on mitochondrial respiration in suspensions of isolated mitochondria showed that PCE and TCVG are more toxic in renal mitochondria from male rats than in those from female rats. Respiratory function in (renal) mitochondria from mice was significantly inhibited by PCE and TCVG, but showed little sex dependence *(49)*. Experimental data showed that TCVG formation in kidney and liver subcellular fractions from male rats and mice were invariably higher than corresponding values in female rats and mice *(53)*.

Elimination

In humans and animals, the major part of the absorbed amount of PCE is exhaled unchanged. In humans, 80–100% of the uptake was exhaled as parent compound in the 7 days following a single 4-hour inhalation exposure to 488 or 976 mg/m^3 (72 or 144 ppm) PCE. In rats, the proportion is somewhat lower (68%). Elimination of PCE from adipose tissue is relatively slow (calculated half-life 55 hours) owing to the high adipose/blood partition coefficient and the low rate of blood perfusion to this tissue *(2)*. Excretion of metabolites in urine represents only a small proportion of the inhaled dose. Following single inhalation exposure in humans, only 2% of the uptake was found as the major urinary metabolite, tetrachloroacetic acid. This compound was excreted from the blood with a half-life of 75–80 hours. In another study, its half-life in urine was estimated at 6 days *(16)*.

In a study in which humans were exposed by inhalation to 6.8 mg/m^3 (1 ppm) PCE in the air for 6 hours, the average recovery by exhalation was calculated to be 82%. This implies that about 18% was metabolized. PCE was readily detected in alveolar air and venous blood; trichloroacetic acid was found in venous blood and urine. Recovery was primarily through exhaled air; only a small amount (less than 1% of intake) of trichloroacetic acid was excreted via the urine. Between about 63% and 93% of the intake was exhaled as parent compound 6 days after the exposure; 0–10% was estimated to be exhaled as PCE after the 6-day period *(57)*. An inhalation study in humans and rats exposed for 6 hours at different concentrations of PCE showed excretion of trichloroacetic acid and the acetylated metabolite N-acetyl-TCVC in the urine of both species. Excretion of the N-acetyl-TCVC was significantly higher in male than in female rats *(54)*.

In rat studies, high concentrations in the milk have been observed, peak concentrations being an order of magnitude higher than in maternal blood *(58)*. Experimental data in lactating goats showed that, following intraruminal admin-

istration of an equal volume mixture of PCE, TCE and methyl chloroform, the milk secreted during the 24 hours following the administration contained 6.43 mg PCE (in addition to TCE and methyl chloroform). PCE demonstrated the greatest tissue partitioning compared to TCE and methyl chloroform, being persistently in the blood and secreted into the milk *(59)*. Limited data in humans also show that PCE is excreted in the milk *(60)*.

Biomarkers of exposure

Biological monitoring of exposure to PCE can be carried out by measuring levels of the parent compound in blood, urine or exhaled air or of the metabolites in blood or urine. These methods have been applied for assessing both occupational and non-occupational exposure.

There has been discussion in the literature as to whether measurement of the parent compound in blood or in exhaled air is the preferred biological index to monitor PCE exposure *(47,61–63)*. A study in humans showed that correlation coefficients (r) between environmental PCE and PCE-B (PCE measured in blood), PCE-Alv (PCE measured in alveolar air) and PCE-U (PCE measured in urine) were 0.94, 0.81 and 0.67, respectively. A high correlation was also found among biological indices: the r value was 0.96 between PCE-B and PCE-Alv, 0.95 between PCE-B and PCE-U, and 0.87 between PCE-Alv and PCE-U *(61)*. The examined biological indices proved sensitive enough for biological monitoring of low exposure to PCE and can give substantially similar information in terms of exposure evaluation. PCE measurement in alveolar air offers some practical advantages over the other exposure indices.

Measuring of metabolites (trichloroacetic acid, trichlorethanol) in blood or urine may not necessarily represent exposure to PCE because some related chlorinated hydrocarbons (TCE, 1,1,1-trichloroethane) are converted to the same metabolites *(2)*.

Physiologically based pharmacokinetic modelling

Several groups of researchers have developed PBPK models for PCE and several of the models have been evaluated. Table 9.1 provides an overview of these efforts *(41,46,58,60,64–79)*.

Most PBPK models for PCE share the four-compartment structure (liver, fat, rapidly perfused tissues and slowly perfused tissues) and steady-state description of lung equilibration developed by Ramsey & Andersen *(80)* for styrene. Only one of the published models *(71)* provides a description of the kinetics of trichloroacetic acid, the major metabolite of PCE.

Some studies have focused on the evaluation of these models. In one, the key parameters and predictions for PBPK models for mice, rats and humans developed by different groups of researchers were compared. The amounts of metabolized PCE predicted showed considerable differences (about 12- to 14-fold for

humans). Most of the differences in risk-related model predictions were due to the choice of the data sets used for calibrating metabolic parameters (V_{max}, K_m) *(77,81)*. A statistical approach to some of the PBPK models for PCE in mice, rats and humans showed that the kinetic parameters defining the metabolic rate were the most important parameters for model sensitivity *(82)*.

Health effects

Identification of studies

Epidemiological studies on health effects of PCE exposure were identified from electronic searches and hand searches of references in former reviews by WHO. Electronic searches were made in PubMed in July 2008, with an update in June 2009. We intended to identify all studies with original data on health effects of PCE and the main descriptors used were "tetrachloroethylene" and "perchloroethylene". In addition, studies that examined the health effects of PCE were identified through hand searches of earlier reviews of the topic, citations within papers identified on health effects of PCE and searches on the web sites of international or national health assessment agencies, including WHO, the European Commission, Health Canada, IARC, ATSDR, USEPA, the United Kingdom Committee on Carcinogenicity of Chemicals in Food, Consumer Products and the Environment and the US National Institute for Occupational Safety and Health. Papers known to the expert group in 2009 concerning health effects of PCE were also used.

Of 148 papers identified, 59 were relevant to the health effects section of this chapter. These papers were included in the discussion presented below, addressing human exposure and epidemiological issues (37), children (0), animal studies (10), cell studies (4), reviews (4) and other studies (4). In addition, 11 reports of the above-mentioned agencies were used in the "Health effects" section.

Effects on experimental animals and in vitro test systems

Toxicological effects

PCE has a low acute inhalation toxicity (LC_{50} in rodents ≥ 16.6 mg/litre). Acute oral toxicity is also low (LD_{50} in rodents ≥ 3000 mg/kg body weight) *(6)*.

The liver, kidneys, blood and CNS are the target organs for systemic effects. Hepatic effects occur at lower dose levels in mice than in rats. In a series of experiments in mice, continuous (24 hours/day) inhalation exposure for 30 days at concentrations of 61, 251, 508 or 1017 mg/m^3 produced a dose-related increase in liver weight at all dose levels. Morphological changes in the liver were observed at 251 mg/m^3 and, as stated but not fully reported, at all other dose levels as well. Plasma butyrylcholinesterase activity showed a slight increase at ≥ 251 mg/m^3. The reversibility of the effects was examined at 1071 mg/m^3 only, showing that at 120 days after cessation of treatment, only a slight increase in liver weight remained *(83)*.

Table 9.1. Physiologically based pharmacokinetic (PBPK) models for PCE metabolism

Species	Input parameters and calibration
Mice, humans	Data from single-dose inhalation
Humans	Partition coefficients determined in vitro; metabolic parameters from occupational studies
Mice, rats	Partition coefficients determined in vitro; metabolic parameters from oral and/or inhalation exposure studies in rats and mice
Humans	Animal data and metabolic parameters derived from data on urinary levels of trichloro compounds in urine of workers exposed to PCE
Rats, humans	Partition coefficients determined in vitro; metabolic parameters calculated and optimized from inhalation studies in rats and humans
Rats (male)	Partition coefficients and metabolic parameters from data generated by a single intra-arterial dose study in male rats
Rats (male), dogs (male)	Partition coefficients from AUCs[a] as determined in vivo in single-dose oral tests in rats and dogs; metabolic parameters estimated from blood and liver concentrations
Rats (lactating)	Partition coefficients determined in vitro; metabolic parameters from in vivo gas-uptake tests in lactating rats
Humans (lactating)	Existing model adjusted for prediction of excretion of PCE in mother's milk
Humans	Assess an existing PBPK model; metabolic parameters from in vivo experiment in Orientals and Caucasians
Mice	Partition coefficients determined in vitro; metabolic parameters from in vivo gas-uptake tests and Monte Carlo analysis to estimate variability
Humans	Describe the relationship between individual and population physiological parameters by using an existing PBPK model in a Markov chain Monte Carlo (MCMC) analysis; metabolic parameters from an existing in vivo inhalation study
Rats, mice, humans	Validate an existing PBPK model and develop a refined one; metabolic parameters from in vivo and in vitro experiment
Rats	Develop a PBPK model; metabolic parameters from mixed exposure in vivo experiments
Humans	Validate and calibrate an existing PBPK model; anatomical, physiological, biochemical and physicochemical data from literature
Rats, humans	Percutaneous permeability coefficients determined in dermal exposure experiments (in vivo)
Humans	Calibrate single PBPK models and describe metabolic interactions; metabolic data from inhalation exposure studies in rats and humans
Humans, rats	Evaluate and compare existing PBPK models and develop a refined one; metabolic parameters from oral and inhalation exposure studies in rats and humans
Humans	Describe the relationship between individual and population physiological parameters by using an existing PBPK model in an updated MCMC analysis; metabolic parameters from an existing in vivo inhalation study
Humans	Characterize the uncertainty and variability of metabolized fraction by using a modified PBPK model in an MCMC analysis; metabolic parameters from several existing in vivo inhalation studies.

[a] AUC = area under the curve.

Model application	Reference
Human cancer risks estimated on the basis of the predicted amounts of PCE metabolites in mice and humans, and using liver tumour incidences in mice	Chen & Blancato *(64)*
Simulation of the time-course of PCE concentration in blood for continuous inhalation exposure	Bogen & McKone *(65)*
Simulation of the amount of urinary metabolites in mice or proportion of exhaled PCE following a single inhalation exposure in rats	Ward et al. *(66)*
Simulation of the time-course of exhaled unchanged PCE	Ward et al. *(66)*
Simulation of the proportion of exhaled PCE and body burden in rats and humans	Koizumi *(67)*
Simulation of the time-course of concentrations in tissues, blood and exhaled air	Dallas et al. *(41,46)*
Simulation of the time-course of the fractions exhaled and metabolized in single-dose studies in rats and dogs	Dallas et al. *(68,69)*
Simulation of the time-course of PCE concentrations in maternal blood and milk and in pup tissues	Byczkowski et al. *(58)*
Concentrations in milk and infant doses predicted for inhalation exposure scenarios in and close to dry cleaning shops	Schreiber *(60)*
Study ethnic differences in biological monitoring to improve reliability of bio-monitoring (and setting biological limit values)	Jang & Droz *(70)*
Simulation of variability of PBPK model parameters and their effects on PBPK model predictions in risk assessment	Gearhart et al. *(71)*
Estimate the population variability of human PCE metabolism	Bogen & McKone *(65)*
Carcinogenic risk assessment based on amounts of PCE metabolites formed in the livers of rodents and humans	Reitz et al. *(72)*
Investigate pharmacokinetic interactions among PCE, TCE, methyl chloroform; assessment of occupationally relevant exposures at or below threshold limit values	Dobrev, Andersen & Yang *(73)*
Analyse human exposure data and predict urinary excretion of trichloroacetic acid	Loizou *(74)*
Assessment of dermal absorption from a soil matrix and evaluation of skin compartment models	Poet et al. *(75)*
Evaluate metabolic interactions (and thresholds) between PCE, TCE and 1,1,1,-TCE	Dobrev, Andersen & Yang *(76)*
Simulation of urinary excretion of trichloroacetic acid at low concentration exposures	Clewell et al. *(77)*
Estimate the population variability of human PCE metabolism	Chiu & Bois *(78)*
Estimate the population variability of human PCE metabolism	Covington et al. *(79)*

Within the United States National Toxicology Program (NTP) subchronic inhalation studies were carried out in rats and mice. In mice, liver effects were observed at 1350 mg/m^3 (≥ 200 ppm) or higher. Karyomegaly of the renal tubule epithelial cells was observed at ≥ 1350 mg/m^3 (≥ 200 ppm). At 680 mg/m^3 (100 ppm), no effects were seen but at this level no histopathological examination of the liver was carried out. In rats, mild congestion of the liver was seen at ≥ 1350 mg/m^3 (≥ 200 ppm) (lower concentrations not tested), with congestion of the lungs, decreased survival and growth retardation at higher dose levels *(84)*. In chronic studies, renal tubular cell karyomegaly was observed in female rats and mice at both 1356 and 2712 mg/m^3 (200 and 400 ppm) in rats and 678 and 1356 mg/m^3 (100 and 200 ppm) in mice.

In addition, in rats, renal tubular hyperplasia (males), thrombosis and squamous metaplasia in the nasal cavity (males and females) and hyperlasia in the adrenal medullae (males) or cortices (females) were found. In mice only, liver cell degeneration and necrosis were seen at both concentrations *(84)*. A study exposing mice to 2040 mg/m^3 (300 ppm) perchloroethylene gas for 6 hours daily for 5 days revealed regeneration of olfactory mucosa. Two weeks and three months after exposure, the nasal mucosa was examined histopathologically. After two weeks, ciliated epithelium started to replace the olfactory epithelium. Damage was more persistent in the nasal mucosa of the olfactory region than in the respiratory region *(85)*.

CNS effects have been observed at high dose levels. In the short-term NTP experiment in rats and mice, neurological symptoms were observed only at the highest concentration of 11 860 mg/m^3 (1750 ppm) *(84)*. Biochemical changes in brain tissues have been observed in rats and gerbils at concentrations of ≥ 407 mg/m^3 (≥ 60 ppm). However, the toxicological significance of these changes is unclear *(2)*. In a recent short-term study in rats, decreased weight of brain regions and reductions in neuronal marker proteins were seen at 4080 mg/m^3 (600 ppm) but not at 2040 mg/m^3 (300 ppm) *(86)*. Haematotoxicity was observed in an inhalation study in mice at test concentrations of 915 and 1830 mg/m^3 (no other concentrations tested) in which the animals were exposed for 6 hours/day, 5 days/week for 7.5 or 11.5 weeks *(87)*. Rats that were acutely exposed to a high dose (500 mg/kg oral) of PCE and others subchronically to lower doses (5 and 50 mg/kg oral), showed significant effects on nociception and locomotor activity *(88)*. An inhalation study assessed the effects of PCE on sustained attention in rats performing a visual signal detection task. It showed that inhaled PCE acutely impaired sustained attention in rats, and its potency weakened on repetition of the exposure. Accuracy was significantly reduced at 3390 mg/m^3 (500 ppm), significantly elevated response time was seen at 6780 mg/m^3 (1000 ppm) and significantly reduced trial completions were found at 10 170 mg/m^3 (1500 ppm) *(89)*.

Limited teratogenicity studies in rats, mice and rabbits suggest that PCE produces fetotoxicity and embryotoxicity at high dose levels (≥ 2034 mg/m^3). In a

behavioural teratogenicity study in rats, neuromuscular ability in pups was decreased at 6100 mg/m^3 (900 ppm) but not at 2034 mg/m^3 (300 ppm) *(2)*. In a study on developmental toxicity, embryos from rats were explanted on gestational day 120 and cultured for 46 hours in the presence of PCE. Exposure to PCE ranging from 3.5 to 15 mM caused concentration-related effects on growth and development. The presence of hepatic microsomal fractions in the culture medium partially prevented the effects of PCE on the measured parameters of embryo growth and development *(90)*. A study showed altered behaviour in adult mice orally exposed to PCE as neonates (5 and 320 mg/kg PCE/day between days 10 and 16 postnatally), indicating neonatal susceptibility of brain maturation in achieving long-lasting changes in adult behaviour *(91)*. A developmental study in rats following inhalation exposure to PCE showed maternal responses that were of limited toxicological significance. Developmental effects at 600 ppm consisted of reduced gravid uterus, placental and fetal weights and decreased ossification of thoracic vertebral centra. Developmental effects at 1695 mg/m^3 (250 ppm) were of minimal toxicological significance, being limited to minor decreases in fetal and placental weights. There were no developmental effects at 441 mg/m^3 (65 ppm) *(92)*.

PCE at 68–2043 mg/m^3 (10–300 ppm) was found to increase, in a concentration-dependent manner, ACh- and high K+-induced muscle contraction in tracheal tissue from swine. Swine tissue was used because there are many similarities between swine and human airways. More research is necessary to be able to conclude that these responses play a role in airway impairment and hyperresponsiveness after PCE exposure *(93)*. A study using renal cell suspensions of rats and mice showed that PCE caused acute renal cellular toxicity in rats and mitochondrial toxicity in rats and mice *(49)*.

Carcinogenic effects

Data on the carcinogenicity of PCE have been evaluated in various health assessment documents *(2,6,51)*. PCE-induced nephrotoxicity and nephrocarcinogenicity have been associated with metabolism by the glutathione conjugation pathway to form TCVG *(48,53)*.

Oral and inhalation studies with NTP have been performed in mice and rats. In a gavage study in B6C3F1 mice (time-weighted average (TWA) daily dose levels of 536 and 1072 mg/kg body weight in males and 386 and 772 mg/kg in females), increased incidences of hepatocellular carcinomas were found in males and females (4/37, 32/49 and 27/48 in males and 2/40, 19/48 and 19/48 in females). In Osborne Mendel rats, no increase in tumour incidence was seen. This study has various limitations: numerous dose adjustments during the study, early mortality related to compound-induced toxic nephropathy, and pneumonia due to intercurrent infectious disease in both rats and mice *(2,94)*. In the inhalation study in B6C3F1 mice (test concentrations 100 and 200 ppm, 6 hours/day,

5 days/week for 103 weeks, corresponding to 680 and 1360 mg/m^3), incidences of hepatocellular carcinomas were increased (7/49, 25/49 and 26/50 males and 1/48, 13/50 and 36/50 females). In F344/N rats (test concentrations 200 and 400 ppm, 6 hours/day, 5 days/week for 103 weeks, corresponding to 1360 and 2720 mg/m^3), PCE caused dose-related increases in the incidence of stage 3 mononuclear cell leukaemia in animals of both sexes: in males, 20/50 in controls, 24/50 at the low dose and 27/50 at the high dose; in females, 10/50, 18/50 and 21/50, respectively. The historical control for mononuclear cell leukaemia in rats in the same laboratory was 47% in males and 29% in females. Uncommonly occurring renal tubular cell adenomas or adenocarcinomas were found in male rats (adenomas,1/49 in controls, 3/49 at the low dose and 2/50 at the high dose; adenocarcinomas, 0/49, 0/49 and 2/50, respectively).

Although induction of peroxisome proliferation as a mechanism underlying the hepatocarcinogenic effect of PCE in mice appears attractive, a poor quantitative correlation was seen between peroxisome proliferation and tumour formation in the liver following administration by inhalation.

The induction of kidney tumours observed in male rats provides only weak evidence for (human) carcinogenicity. The observed increase in incidence is not statistically significant. In addition, two different mechanisms of action have been proposed for the induction of these tumours: alpha 2μ-globulin nephropathy, an effect specific for male rats, and formation of genotoxic metabolites in the kidneys as the final step of the glutathione biotransformation pathway. Given the low incidences observed, combined with the data on the mechanism of induction, it can be concluded that the result in male rats is equivocal evidence only for a risk of renal cancer in humans.

A review of six carcinogenicity studies of PCE in rats concluded that evidence of increases in mononuclear cell leukaemia has been seen in two studies in the F344 rat but not in other strains, and that as a rat-strain-specific effect it is not considered to be relevant to the evaluation of human cancer risk *(95)*.

IARC *(96)* has concluded that the results of the available animal bioassays provide sufficient evidence for carcinogenicity in animals.

Mutagenicity

Comprehensive reviews are available of the data obtained from the many studies carried out with PCE *(2,51,96)*. In vitro studies include tests for gene mutations in prokaryotes and eukaryotes and tests for chromosome aberrations in mammalian cell lines. In vivo studies include tests for chromosome aberrations in bone marrow in rats and mice and a dominant-lethal assay in rats. In addition, several studies have been carried out on DNA damage in vitro and in vivo. The body of results shows absence of mutagenicity of PCE in virtually all of the systems tested. The few weakly positive results may be due to the presence of mutagenic stabilizers in the test samples *(2,51)*. Binding of PCE in vivo to unpurified

DNA from several organs was noted in one study, although no covalent binding to purified hepatic DNA could be demonstrated in another. In the other available in vivo studies, it is not known whether the test compound (or its metabolites) reached the target tissues. This observation reduces the value of the negative results observed. Nevertheless, an in vivo study, in which male mice were administered PCE intraperitoneally, assessed the induction of micronuclei in hepatocytes and reticulocytes and showed that PCE might have a clastogenic effect in hepatocytes *(97)*. For the metabolites of PCE that are formed by conjugation with glutathione (a minor biotransformation route demonstrated in rodents), positive results were obtained in in vitro studies in *S. typhimurium* TA 100 (reverse mutation), with metabolic activation with kidney microsomes, in the presence of glutathione and glutathione transferase *(96)*.

Interactions with other chemicals

Results of studies on the influence of ethanol on the metabolism and toxicity of PCE in liver did not show synergism *(2,98)*. Increased urinary excretion of metabolites of PCE and enhanced hepatotoxicity have been observed in rats following pretreatment with polychlorinated biphenyls *(2)*. Simulation of interaction thresholds for human exposure to mixtures of TCE, PCE and 1,1,1-trichloroethane was done with PBPK models. Model simulations indicated that during combined exposures, certain toxicological effects may be expected to occur at lower exposure levels compared with PCE exposure alone *(73,99)*.

Effects on humans

Exposure to PCE can affect the CNS, eyes, kidney, liver, lungs, mucous membranes and skin. CNS effects have been most frequently noted *(44)*.

The odour threshold in air for detection of PCE is 8 mg/m^3. The odour threshold in air for recognition of PCE is 3–4 times higher *(16)*.

Acute poisoning incidents

Acute exposure to PCE at air levels of 100–200 ppm can cause irritation of the skin, eyes and upper respiratory tract. Non-cardiogenic pulmonary oedema, nausea, vomiting and diarrhoea can occur. CNS effects have also been observed with acute inhalation exposure to PCE at 50–300 ppm. At these levels, neuromotor effects may be seen and results of certain coordination and behavioural tests may be abnormal. At higher air concentrations, loss of consciousness can occur *(44)*.

Several acute PCE intoxications have been reported. In one case, up to 16 mg was ingested by a 6-year-old boy weighing 22 kg. He was admitted to hospital one hour after ingestion, where his condition deteriorated from somnolence to coma. The initial blood level was 21.5 μg/ml. He recovered completely without liver, renal or CNS injury and was discharged on day 9 *(100)*. In another report,

a 32-year-old man became semi-comatose and experienced oliguric acute renal failure after accidental ingestion of 75 g PCE. A renal biopsy performed on the 19th day after ingestion showed severe acute tubular necrosis. He regained normal renal function after five haemodialyses and conservative treatment. The amount of PCE in the blood and urine were not measured *(101)*.

Three fatalities due to inhalation of PCE have been reported in the literature. A concentration of 4.5 mg/l was measured in the blood of a man aged 53 years weighing 70 kg, who died while he was cleaning and recycling PCE by distillation *(102)*. A two-year-old boy died due to PCE that had been retained in the curtains of his bedroom. A concentration of 66 mg/l blood was measured *(103,104)*. Finally, a 33-year-old man clearing a line in a dry cleaning establishment died with a blood concentration of 44 mg/l *(105)*. A fatality due to poisoning by both PCE and TCE has been described, a 45-year-old woman being discovered unconscious and in cardiac arrest in a laundry area. Examination revealed that she was deeply comatose and had acute respiratory distress syndrome and severe metabolic acidosis. Cardiovascular instability and acute renal failure occurred and eventually the patient died; the results of the autopsy are described in the paper. The blood levels of PCE 2, 4, 5, 6 and 7 days after hospital admission were respectively 1319, 758, 787, 436 and 656 μg/l *(106)*.

Effects on the CNS

Depending on the concentration, acute exposure can result in loss of coordination, reversible mood and behavioural changes, or potentially anaesthetic effects. People chronically exposed to PCE may experience ataxia, disorientation, irritability, peripheral neuropathy, short-term memory deficits and sleep disturbance. Reversibility depends on the degree of severity of the exposure and associated effects *(44)*.

PCE has been associated with neurobehavioural dysfunction, including reduced attention in humans. In a series of controlled short-term studies in limited numbers of human volunteers, neurological symptoms (including dizziness, drowsiness and decreased functioning in motor coordination tests) and visual system dysfunction were observed at ≥ 678 mg/m^3 (≥ 100 ppm) and 339 mg/m^3 (50 ppm), respectively *(2,16,107,108)*. Limited information on neurological effects following long-term exposure was obtained in occupational studies in dry cleaning workers. In a cross-sectional study with two groups of exposed workers (exposure concentrations 83 ± 53 mg/m^3 and 364 ± 114 mg/m^3, duration of exposure 127 or 141 days), small effects on scores in psychological tests were found. However, the response did not correlate with the exposure level in this study *(2,6,109)*.

In another study in female dry cleaning workers with exposures of 6.8–408 mg/m^3 (4-hour averages, median 102 mg/m^3) and PCE concentrations in the blood of 12–864 mg/l (median 145 mg/l), performance test scores in a test bat-

tery for neuromotor functions were decreased. Neither duration of exposure nor blood concentration of PCE was significantly correlated with performance *(110)*. In cross-sectional studies in dry cleaning workers, effects on blue–yellow colour vision were found at mean PCE concentrations of 42–102 mg/m^3 *(111,112)*. In Italy, PCE-induced impairment of colour vision was studied in 33 dry cleaning workers. Exposure was evaluated with passive samplers and colour vision was assessed. Two years later, the workers were re-examined. The exposure to PCE had increased in subgroup A (median 1.7 ppm vs 4.3 ppm). In subgroup B, exposure was reduced (median 2.9 ppm vs 0.7 ppm). Colour vision worsened in subgroup A but no vision changes were noticed in subgroup B, indicating that an increase in exposure during a 2-year period can cause colour vision to deteriorate *(113)*.

A case report described a 57-year-old woman exposed to supposedly high concentrations of PCE while working at a dry cleaning shop, who suffered from blindness for 9 days in the left eye and 11 days in the right eye with optic neuritis. Blood concentrations of PCE 48 and 80 hours after onset of the optic neuritis were respectively 1.08 mg/g and 0.65 mg/g *(114)*.

In a prospective population-based cohort study on 88 829 children, offspring from dry cleaners (144 children) were followed from birth to age 21–33 years. Preliminary findings suggested an increased incidence of schizophrenia (4 cases) in these children *(115)*. However, it should be mentioned that there was no exposure characterization, there were few cases and few details were provided. These findings need to be corroborated in follow-up studies.

Research from 2002 suggests that chronic, environmental exposure to airborne PCE adversely affects neurobehavioural function in healthy individuals. A significantly lower visual contrast sensitivity was reported in apartment residents exposed to PCE (daytime mean 620 μg/m^3, nighttime mean < 100 μg/m^3) compared to unexposed controls. The reliability of these data was later discussed in the literature. Methodological limitations preclude a definitive attribution of causation, and further research is necessary to draw reliable conclusions *(99,116)*.

Effects on the liver

Case reports of human exposure to PCE show that it can cause hepatotoxic effects in humans, which include abnormal liver function tests *(48)*, cirrhosis, hepatitis, hepatomegaly and liver cell necrosis *(44)*. A dose–response relationship in humans for the effects on the liver is not completely known. In case studies of high accidental exposures, effects on the liver have been reported. In limited studies in dry cleaning workers exposed to a TWA concentration of 143 mg/m^3 (21 ppm) over a 6-year period, serum enzymes indicative of liver function were not affected *(62,112)*. A study in dry cleaners frequently exposed to PCE concentrations of 16 ppm (8-hour TWA) revealed mild to moderate hepatic parenchymal changes as determined by hepatic ultrasonography *(117)*.

Renal effects

Nephrotoxic effects have been described in humans *(48,118,119)*. Symptoms of renal dysfunction, including proteinuria and haematuria, have been associated with accidental exposure to anaesthetic concentrations of PCE vapour *(2)*. In several cross-sectional studies in dry cleaning workers, the effect of PCE on renal function was examined. Female workers exposed for an average of 14 years to an estimated TWA concentration of 68 mg/m^3 (10 ppm) had increased urinary levels of lysozyme and ß-glucuronidase suggestive of mild renal effects *(120)*. No effects were observed in workers estimated to have been exposed to a TWA concentration of 142 mg/m^3 (21 ppm) for 6 years *(62)*. In a cross-sectional study, about 20 markers of early nephrotoxic effects were measured in workers in dry cleaning facilities (n = 50). Exposure was determined by analysing air samples collected during 4-hour periods randomly selected over the working week. The median exposure concentration was 102 mg/m^3 (range, trace–580 mg/m^3). Compared to the control population, the exposed group had significantly higher frequencies of abnormal values for a number of the markers in urine, including albumin, transferrin, tissue-nonspecific alkaline phosphatase and brush-border antigens. The significance of the findings cannot be easily assessed but may represent an early stage of clinically silent but potentially progressive renal disease *(118)*. At an average airborne exposure of 8.4 mg/m^3 (range 2.2–44.6), a PCE-related effect on the tubular reabsorption of retinol-binding protein in urine was observed in exposed workers from a dry cleaning shop *(119)*.

Since there are sex- and species-dependent differences in bioactivation and detoxification pathways, more knowledge about the metabolism of PCE in several target organs and in different species is needed to improve human risk assessment *(50)*.

Reproductive and developmental effects

A few epidemiological studies have reported reproductive or developmental abnormalities due to exposure to PCE in drinking-water. The 1998 Camp LeJeune study reported a weak association between PCE exposure due to contaminated drinking-water and birth weight outcomes for small-for-gestational age births. Stronger associations were observed between PCE exposure and birth weight for infants of mothers who were 35 years of age or older and for infants of mothers with a history of fetal death *(121)*. Another study found oral cleft defects associated with PCE-contaminated drinking-water. The authors indicate that this study cannot resolve whether the drinking-water contaminants caused the adverse birth outcomes; these findings should therefore be followed up utilizing available drinking-water contamination databases *(122)*.

In a comment on this paper, it is suggested that the oral cleft defects found are biologically plausible *(123)*. According to these authors, a study of mothers with pregnancies affected by neural tube defects in Dublin *(124)* suggests a mecha-

nism for the induction of neural tube defects related to a metabolic slowdown of the methionine synthase reaction. Recently, two cohort studies examined the effects of prenatal exposure to PCE-contaminated drinking-water on adverse birth outcome and risk of behavioural disorders. It was concluded that prenatal and early postnatal PCE exposure is not associated with disorders of attention, learning and behaviour *(125)*. Further, it was suggested that prenatal PCE exposure does not have an adverse effect on birth weight or gestational duration *(126)*.

The results of several studies have indicated that occupationally exposed women might suffer higher rates of spontaneous abortion *(127–129)*. Exposure was classified by reported work history. A significant effect was found when the work tasks included dry cleaning for at least one hour daily or the women reported handling of PCE at least once a week *(128,129)*. A significantly higher risk was found in operators compared to non-operators *(127)*, but other studies have not found this association *(130,131)*. Furthermore, a case-referent study performed within two cohorts did not give any substantial support to the hypothesis that exposure to PCE at work during pregnancy enhances the risk of adverse pregnancy outcome *(132)*. A retrospective time-to-pregnancy study among Finnish women indicated a reduced ability to reproduce among 20 women exposed to PCE (concentration not clear) for 1–4 days a week or daily by inhalation. It should be noted that the studies have a number of limitations, primarily that exposure concentrations are not available *(133)*.

The Camp Lejeune study of ATSDR *(134)* was not included in this guideline, since an error was made in the exposure classification; these data will be re-analysed by ATSDR at a later stage.

Mutagenic and carcinogenic effects

IARC concluded in 1995 that there is evidence for consistently positive associations between exposure to PCE and the risks for oesophageal and cervical cancer and non-Hodgkin's lymphoma. These associations appear unlikely to be due to chance, although confounding factors cannot be excluded and the total numbers in the cohort studies combined are relatively small. IARC therefore concluded that there is limited evidence for the carcinogenicity of PCE in humans *(96)*.

PCE is reasonably anticipated to be a human carcinogen on the basis of limited evidence from studies in humans and sufficient evidence of carcinogenicity from studies in experimental animals. PCE has been studied by observing laundry and dry cleaning workers, who may also have been exposed to other solvents, especially TCE but also petroleum solvents. In several cohort and proportionate mortality studies, excesses have been reported of lymphosarcomas, leukaemias and cancers of the skin, colon, lung and urogenital tract. Some excess of lymphomas and of cancers of the larynx and urinary bladder was seen in a large cohort of dry cleaners. A familial cluster of chronic lymphocytic leukaemia has also been related to dry cleaning. Although these studies suggest a possible associa-

tion between long-term occupational exposure to PCE and increased lymphatic malignancies and urogenital cancers, the evidence must be regarded as inconclusive because workers were exposed to petroleum solvents and other dry cleaning agents as well as PCE *(135)*.

The results of a study in differently exposed dry cleaners and launderers indicated a reduction in oxidative DNA damage in exposed dry cleaners compared to launderers. The mean value for PCE in the blood of these dry cleaners was 0.078 mg/l, and the TWA was < 5 ppm in air for 17 out of 18 dry cleaners. However, PCE could not clearly be identified as the source of the effect *(136)*. In two studies for genetic effects (sister chromatid exchanges and/or chromosome aberrations) in lymphocytes of occupationally exposed workers, no clear-cut effects were found *(6)*. Another study showed modulation of the expression of some genes related to cancer induction in human cord blood cells *(137)*.

A population-based case-control study was undertaken to investigate the association between breast cancer and PCE exposure from public drinking-water (drinking-water consumption as well as bathing habits were taken into account). The same author performed a more extensive case-control study a few years later. Both studies suggest that women with the highest PCE exposure levels have a slightly to moderately increased risk of breast cancer. Analyses of the same data using a newly constructed personally delivered dose model to make a more accurate estimation of the exposure did not significantly change the subjects' exposure classification *(138–140)*. An association between PCE exposure from public drinking-water and lung cancer and possibly colorectal cancer was suggested, based on another population-based case-control study *(141)*.

A paper from 2003 assessed (based on specified methodological and scientific quality criteria) 44 epidemiological papers that provided reasonable data on up to 17 cancer sites. The authors concluded that no evidence for an association between breast, prostate, skin or brain cancer and exposure to PCE was demonstrated. A relationship between PCE and cancer of the oral cavity, liver, pancreas, cervix and lung was considered unlikely by the authors. Scientific evidence was considered inadequate for laryngeal, kidney, oesophageal and bladder cancers *(142)*.

In 2006, the epidemiological literature since 1990 on occupational chlorinated solvent exposure was reviewed. The paper reviewed 28 studies of PCE, all but 5 of which focused on workers in the dry cleaning industry with few or no other chemical exposures. Within the study populations with multiple exposures, three studies found some increased risk of biliary and liver or brain cancer; in the other studies, no increased risk for renal cell carcinoma or for any cancer was found. Census records for those working as a "dry cleaner or laundry worker" or from a database of those being monitored for PCE exposure were linked to cancer registries (three studies) and statistically significant increased risks for liver and pancreatic cancer, Hodgkin's lymphoma and leukaemia were found. In general,

findings in occupational cohort studies have not been consistent, even within the same industries *(143)*.

Health risk evaluation

Critical health outcomes

The main health effects of concern are local irritation (eyes, mucous membranes, respiratory tract and skin), effects on the CNS and cancer. Effects on the liver and kidneys have also been reported.

CNS effects and local irritation

The evidence is sufficient to conclude that PCE can cause irritation of mucous membranes and the respiratory tract. These effects generally occur at high concentrations. Acute exposure to PCE at air levels of 680–1360 mg/m^3 (100–200 ppm) can cause irritation of the skin, eyes and upper respiratory tract in humans. Moreover non-cardiogenic pulmonary oedema, nausea, vomiting and diarrhoea can occur. CNS effects have been observed at high dose levels in rats and mice. In humans, CNS effects have also been observed with acute inhalation exposures of 340–2040 mg/m^3 (50–300 ppm) of PCE. The evidence is sufficient to conclude that there is an association between PCE and CNS effects at sufficiently high concentrations. Since high concentrations typically do not occur in indoor environments for a long period of time, these end-points are not taken into account when setting the guideline value.

Liver and kidney effects

The evidence of an association between PCE exposure and effects on the liver is suggestive. Hepatic effects have been observed in rats and mice in subchronic studies. Case reports of accidental exposures of humans to PCE confirm that hepatotoxic effects can occur in humans, including abnormal liver function tests, cirrhosis, hepatitis, hepatomegaly and liver cell necrosis.

There is suggestive evidence of an association between PCE exposure and effects on the kidneys. In chronic studies, renal effects were observed at 1360 and 2710 mg/m^3 (200 and 400 ppm) in rats and at 680 and 1360 mg/m^3 (100 and 200 ppm) in mice. Reversible kidney damage in humans (e.g. proteinuria and haematuria) has been associated with accidental exposure to acutely toxic concentrations of PCE vapour. A long-term exposure study showed that renal effects may develop at lower concentrations, with the reported onset of renal damage occurring following exposure to a median concentration of 102 mg/m^3 (range, trace–576 mg/m^3).

Reproductive and developmental effects

A few epidemiological studies have reported developmental abnormalities due to PCE exposure in drinking-water (reduced birth weight and oral cleft defects).

Other studies concluded that prenatal PCE exposure does not have an adverse effect on birth weight or gestational duration. Some studies have consistently indicated that occupationally exposed women might suffer higher rates of spontaneous abortion, while others found no association. All the above-mentioned studies have limitations, primarily that the exposure concentrations are not available. Therefore the evidence stays suggestive.

Cancer risk

IARC concluded that the results of the available animal bioassays provide sufficient evidence for carcinogenicity to animals. In these studies, an increased incidence of adenomas and carcinomas was observed in the livers of exposed mice. There is suggestive evidence from mechanistic studies that humans are likely to be less sensitive to the development of these tumours following PCE exposure. A low incidence of kidney tumours among male rats has been reported.

It can be concluded from this small and statistically non-significant increase, together with the data relating to the possible mechanism of induction, that the result in male rats is equivocal evidence only for a risk of renal cancer in humans.

The significance for humans of the increased incidence of mononuclear cell leukaemia, as observed in two studies in F344 rats, is unclear. This is due to the lack of understanding of the mechanism underlying the formation of this cancer type (which has a high background incidence) and the suggestion that it might be a rat-strain-specific effect.

IARC concluded in 1995 that there is evidence for consistently positive associations between exposure to PCE and the risks for oesophageal and cervical cancer and non-Hodgkin's lymphoma.

These associations appear unlikely to be due to chance, although confounding factors cannot be excluded and the total numbers in the cohort studies combined are relatively small.

A paper from 2003 assessed (based on specified methodological and scientific quality criteria) 44 epidemiological papers that provided reasonable data on up to 17 cancer sites. The authors concluded that no evidence for an association between breast, prostate, skin or brain cancer and exposure to PCE was demonstrated.

A relationship between PCE and cancer of the following sites was considered unlikely by the authors: oral cavity, liver, pancreas, cervix and lung. Scientific evidence was considered inadequate for laryngeal, kidney, oesophageal and bladder cancers. Since then, new studies have been published, but the evidence concerning the carcinogenicity of PCE is still not conclusive. The evidence for an association therefore remains suggestive.

From the weight of the evidence from mutagenicity studies, there are no indications that PCE is genotoxic. Although several in vitro studies indicate that

conjugation of PCE with reduced glutathione (a minor biotransformation route demonstrated to occur in rodents) produces renal metabolites that are mutagenic in *S. typhimurium* TA 100, the significance of the latter results for humans is doubtful. In two studies investigating genetic effects (sister chromatid exchanges and/or chromosome aberrations) in lymphocytes of occupationally exposed workers, no clear-cut effects were found.

In conclusion, carcinogenicity is not used as an end-point, since there are no indications that PCE is genotoxic and there is some uncertainty about the epidemiological evidence as well as the relevance of the animal carcinogenicity data to humans. However, because of the remaining uncertainty about the carcinogenicity of PCE, it should be kept under review.

Health relevance of current indoor exposures

Inhalation of PCE is the major route of exposure in the general population. Ambient air concentrations of PCE are generally < 5 μg/m^3 in urban areas and typically < 1 μg/m^3 in rural areas. Indoor concentrations are generally well below 20 μg/m^3, with median concentrations ranging from 0.16 to 8.7 μg/m^3 in the described studies. These concentrations are an order of magnitude below concentrations that can be relevant for health.

Indoor PCE air levels may be up to 5.0 mg/m^3 (4–24-hour average) in buildings with dry cleaning operations where PCE is used. There is sufficient evidence to conclude that concentrations in premises next to dry cleaning operations can exceed safe concentrations. This should be the focus of concern.

Conclusions of other reviews

IARC concluded that there is evidence for consistently positive associations between exposure to PCE and the risks for oesophageal and cervical cancer and non-Hodgkin's lymphoma. PCE is classified by IARC as a Group 2A carcinogen (probably carcinogenic to humans) *(96)*.

The EU classified the substance as carcinogenic category 3 (substances that cause concern for humans owing to possible carcinogenic effects but in respect of which the available information is not adequate for making a satisfactory assessment) and risk phrase 40 (limited evidence of a carcinogenic effect) *(144)*.

USEPA does not currently have a classification for the carcinogenicity of PCE but has calculated a provisional inhalation unit risk estimate of 5.8×10^{-7} (μg/m^3)$^{-1}$. A provisional value is one that has not received Agency-wide review *(145)*.

The United Kingdom Committees on Toxicity, Mutagenicity and Carcinogenicity of Chemicals in Food, Consumer Products and the Environment concluded that there was "no satisfactory epidemiological evidence to associate PCE exposure to cancer in the available cohort studies" *(146)*.

The US National Institute for Occupational Safety and Health considers PCE to be a potential occupational carcinogen *(147)*.

ATSDR has derived both an acute inhalation minimal risk level (MRL) of 1.38 mg/m^3 (0.1 ppm) and a chronic inhalation MRL of 0.28 mg/m^3 [1] (0.04 ppm) *(2)*.

Guidelines

Carcinogenicity is not selected as the end-point for setting the guideline value for three reasons: the epidemiological evidence is equivocal, the animal tumours detected are not considered relevant to humans, and there are no indications that PCE is genotoxic. The derivation of a guideline value is at present based on two non-neoplastic effects as the critical end-point: impaired neurobehavioural performance and early renal changes.

On the basis of a long-term LOAEL for kidney effects of 102 mg/m^3 in dry cleaning workers, a guideline value of 0.25 mg/m^3 has been calculated. In deriving this guideline value, the LOAEL is converted to continuous exposure (dividing by a factor of 4.2 (168/40)) and divided by an uncertainty factor of 100 (10 for use of a LOAEL and 10 for intra-species variation). Recognizing that some uncertainty in the LOAEL exists because the effects observed at this level are not clear-cut and because of fluctuations in exposure levels, an alternative calculation was made based on the LOAEL in mice of 680 mg/m^3 and using an appropriate uncertainty factor of 1000. This calculation yields a guideline value of 0.68 mg/m^3.

A chronic inhalation MRL of 0.28 mg/m^3 (0.04 ppm) has been derived by ATSDR based on the LOAEL of 15 ppm identified in the Ferroni study *(110)*. The MRL was calculated from this concentration by expanding to continuous exposure (8/24 hours, 5/7 days) and dividing by an uncertainty factor of 100 (10 for use of a LOAEL and 10 for human variability). This reference found significantly prolonged reaction times in workers occupationally exposed to an average of 15 ppm for about 10 years *(2,110)*.

The value and appropriateness of establishing a short-term guideline value is questionable because acute effects occur only at very high concentrations of 50 ppm (340 mg/m^3) and higher, compared to generally observed levels in close proximity to dry cleaning facilities. Establishing a long-term value is more protective of human health.

On the basis of the overall health risk evaluation, the recommended guideline for year-long exposure is 0.25 mg/m^3. This is the same as the previous WHO guideline *(148)*.

The guidelines section was formulated and agreed by the working group meeting in November 2009.

[1] This figure was calculated and found to be 0.24 mg/m^3 using the information provided by ATSDR. This may be due to a different conversion factor for converting ppm to mg/m^{3}and rounding during the calculation.

Summary of main evidence and decision-making in guideline formulation

Critical outcome for guideline definition

Effects in the kidney indicative of early renal disease and impaired neurobehavioural performance. Carcinogenicity is not used as an end-point as there are no indications that PCE is genotoxic and there is uncertainty about the epidemiological evidence and the relevance to humans of the animal carcinogenicity data.

Source of exposure–effect evidence

- Based on a health surveillance study of dry cleaning workers exposed to PCE, the long-term LOAEL for kidney effects was considered to be 102 mg/m^3. This was adjusted for continuous exposure by dividing by a factor of 168/40. Further, factors of 10 for use of a LOAEL and 10 for intraspecies variation were incorporated, leading to a guideline value of 0.25 mg/m^3 *(62)*.
- Based on a study of 30 female dry cleaning workers exposed to PCE for an average of 10 years *(110)*, a LOAEL of 103 mg/m^3 (15 ppm) has been derived and a chronic-duration inhalation MRL of 0.28 mg/m^3 (0.04 ppm) calculated.

Supporting evidence

- Several epidemiological studies on renal changes and exposure to PCE, including studies in dry cleaning facilities. The significance of these findings cannot be easily assessed, but may represent a relationship between long-term exposure and effects on the kidney in humans *(48, 118,119, 120)*.
- Associations between PCE exposure and neurobehavioural symptoms were suggested in two studies *(108,109)*.

Results of other reviews

- ATSDR derived a chronic inhalation MRL of 0.28 mg/m^3 (0.04 ppm) *(44)*.
- IARC: Group 2A (probably carcinogenic to humans) *(96)*.

Guideline

0.25 mg/m^3 – annual average.

Comments

No change in the guideline as compared to *Air quality guidelines for Europe (148)*.

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This book presents WHO guidelines for the protection of public health from risks due to a number of chemicals commonly present in indoor air. The substances considered in this review, i.e. benzene, carbon monoxide, formaldehyde, naphthalene, nitrogen dioxide, polycyclic aromatic hydrocarbons (especially benzo[*a*]pyrene), radon, trichloroethylene and tetrachloroethylene, have indoor sources, are known in respect of their hazardousness to health and are often found indoors in concentrations of health concern. The guidelines are targeted at public health professionals involved in preventing health risks of environmental exposures, as well as specialists and authorities involved in the design and use of buildings, indoor materials and products. They provide a scientific basis for legally enforceable standards.

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Public Health England

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Indoor Air Quality Guidelines for selected Volatile Organic Compounds (VOCs) in the UK

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Background

With the UK population spending on average around 80-90% of their time inside buildings, and up to 60% of their time in their homes (Kornartit et al., 2010; Dimitroulopoulou et al., 2017), buildings are important modifiers of population health (Thompson et al., 2013). Poor indoor air quality may cause or aggravate odour and irritation, allergic and asthma symptoms, airborne respiratory infections, chronic obstructive pulmonary disease, cardiovascular disease and lung cancer (Carrer et al., 2009). In addition, the effects of indoor air pollution exposure on school performance, office productivity, comfort and well-being of occupants has become an emerging focus of research (eg Wargocki and Wyon, 2017; Eitland et al., 2018; Gupta et al., 2018) and statutory guidance has recently been published (eg DfE, 2018). Overall exposure levels inside buildings are likely due to pollutants from both indoor and outdoor sources, although some attenuation by buildings occurs. Although there is a plethora of pollutants found indoors, including gaseous pollutants (inorganic chemicals, radon, volatile organic compounds, VOCs), biological pollutants (allergens, viruses and bacteria, mould) and particulate matter, the current work focusses on indoor generated VOCs and the guideline values that would aim at their control in the indoor environment.

According to BS EN16516:2017, *very volatile organic compound* (VVOC) is the volatile organic compound eluting before n-hexane on the gas chromatographic column, as specified in the Standard. *Volatile organic compound* (VOC) is the organic compound eluting between and including n-hexane and n-hexadecane on the gas chromatographic column, as specified in the Standard. *Semi-volatile organic compound* (SVOC) is the organic compound which elute after n-hexadecane, on the gas chromatographic column, as specified in the Standard. *Total volatile organic compounds* (TVOC) is the sum of the concentrations of the identified and unidentified volatile organic compounds, as specified in the Standard. All compounds listed in Annex G of BS EN16516:2017 shall be regarded as VOC, even if they elude from the gas chromatographic system before n-hexane or after N-dexadecane. These include aromatic hydrocarbons, saturated aliphatic hydrocarbons (n, -iso, cyclo-), terpenes, aliphatic alcohols, aromatic alcohols, glycols, glycolethers and aldehydes. Formaldehyde (HCHO) is of greatest importance, due to its prevalence in the indoor environment and its known health impacts (WHO, 2010).

The presence of volatile organic compounds (VOCs) and the associated health risks in residential and public buildings are well reported (eg Sarigiannis et al., 2011). Due to their properties, VOCs are widely used in construction and building products (eg paints, varnishes, waxes, solvents), in household consumer products (detergents, cleaning products, air fresheners and personal care products) and are also emitted while using electronic devices such as photocopiers or printers (eg Missia et al., 2010, Bartzis et al. 2015; Cacho et al., 2013; GEA, 2017). Secondary pollutants can be also formed by ozone-initiated chemistry of terpenes and degradation (eg Nazaroff and Weschler, 2004; Kephalopoulos et al., 2007; Nørgaard et al., 2014). Health Organisations (eg The World Health Organization, The US Environmental

Protection Agency, PHE) have assessed the evidence and listed the health impacts of VOCs, which include irritation of the eyes and respiratory tract, allergies and asthma, central nervous system symptoms, liver and kidney damage, as well as cancer risks.
Given the presence of VOCs in residential and public buildings and their health impacts, prioritisation of the air pollutants and individual VOCs that should be considered for monitoring campaigns and proposing guideline values has been carried out by various researchers (eg COMEAP, 2004; Kotzias et al., 2005 – INDEX project; SCHER, 2007; Carreer et al., 2009 – ENVIE project). These early European projects led to the development of the WHO indoor air quality guidelines for selected pollutants (WHO, 2010), which are intended for use in countries with no relevant regulations. However, there are countries that have made real advances in mitigating indoor air pollution and developed guidelines for the indoor air contaminants in recent years (eg Germany, Canada, Japan and the Flemish Government.).

In the UK, there are currently no indoor air quality guidelines for individual volatile organic compounds. In their absence, the recently revised Department for Education Guidance BB101: Ventilation, thermal comfort and indoor air quality (DfE, 2018) recommended the use of the WHO (2010) Indoor Air Quality (IAQ) guidelines. The current Building Regulations Part F (2010) gives guidance regarding the maximum concentrations of certain pollutants within the building envelope for ventilation purposes (HM Government, 2010). Apart from inorganic pollutants, these include TVOCs. TVOC is used as a measure giving a possible indication of poor/good indoor air quality; furthermore it is proposed as an indicator for the calculation of ventilation rate (eg Hormigos-Jimenez et al., 2017). However, TVOCs reveal little regarding the nature of the individual compounds, their concentrations and their possible toxicity to humans.

Therefore, the overall objective of this work is to carry out a comprehensive literature review to propose indoor air quality guidelines for individual VOCs in the UK. The starting point was the 2010 WHO IAQ guidelines and our objective was to investigate if the proposed individual VOCs and their limit values are still appropriate for use and if new compounds should be considered based on the recent scientific evidence about their toxicity and presence in buildings. A short description of the methodology is given below together with the proposed VOC guidelines, whereas the full details of the work and analysis are presented and discussed in Shrubsole et al. (2019).

Methodology

To target the individual VOCs for which indoor air quality guidelines should be proposed in the UK, we carried out a systematic literature review of the current research evidence on the occurrence of VOCs in the indoor residential and public buildings (offices), mainly in the UK and Europe. The compounds present, their sources and concentrations, their toxicity and health impacts were investigated. The individual VOCs that were identified were further investigated to assess their relevance according to the limits of exposure and their prevalence in residential and office buildings. The VOCs, for which we propose IAQ guidelines, are emitted from construction products and building materials; however, most monitoring studies are carried out post occupancy, and the contribution of VOCs from consumer products represents a large component of individual indoor exposure and are also considered here.

We reviewed existing the evidence base of health-based guidelines proposed by other countries and organisations, to identify which existing guidelines could be adopted for individual VOCs. We did not aim to carry out a full review of the toxicological evidence, to produce new guidelines. For this project, we selected the most appropriate existing health-based guideline values (HBGVs) for inhalation and propose these as UK IAQ guidelines. In the case of naphthalene there is emerging toxicological data that may change proposed guideline values. However, it has yet to be reviewed by an authoritative body (eg PHE, US EPA) and it was outside the scope of this project to derive new HBGVs.

Search

The comprehensive literature search was limited to studies in English published from 2000 to 2018 and included the following aspects and disciplines: building physics, indoor air quality and ventilation, VOC emissions from construction and consumer products, case studies of concentrations for individual VOCs - with a focus on statistically significant/large scale studies, health effects, international guidance on health based domestic concentrations and suggested mitigation strategies. The following electronic databases were investigated: Scopus, including citation reports, Elsevier, Google Scholar, PubMed, Ovid Embase, EBSCO Global Health, TRIP and NICE Evidence. Furthermore, we investigated the grey literature, including European Union, UK and other Government legislative and policy documents, national and international VOC guidelines for indoor air, technical data sheets and specifications, published textbooks, reports from organisations involved in the investigation of VOC emissions from construction products, the refurbishment process, recognised websites (for example from construction organisations).

The comprehensive review is presented and discussed by Shrubsole et al. (2019). The PHE indoor air quality guidelines for selected VOCs in the UK are presented in Table 1.

Table 1 Indoor air quality guidelines for selected VOCs in the UK (µg.m^{-3})

VOCs	Limit Values in µg.m^{-3}		Source Document	Reasoning for choice	Potential Health impacts
	Short Term	Long Term			
Acetaldehyde (75-07-0)	1,420 (1h)	280 (1day)	Health Canada (2018)[a]	Most recent appraisal of evidence	Irritation of the eyes, skin, and respiratory tract following acute exposure.[3] Long-term animal studies have reported carcinogenicity and inflammation and injury to tissues of the upper respiratory tract (Health Canada, 2018)
α-Pinene (80-56-8)	45,000 (30min)	4500 (1 day)	EPHECT (Trantallidi et al., 2015)	Critical Exposure limit (CEL) inhalation exposure to key and emerging indoor air pollutants emitted during household use of selected consumer products	With the exception of its irritative (skin, eyes) and sensitizing properties, it is a chemical with fairly low acute toxicity.[4] Ozone initiated reactions with terpenes produce gaseous and aerosol phase products, causing sensory irritation of upper airways and airflow limitation.
Benzene* (71-43-2)	No safe level of exposure can be recommended. The unit risk of leukaemia per 1µg.m^{-3} air concentration is 6×10^{-6}. The concentrations of airborne benzene associated with an excess lifetime cancer risk of 1/10 000, 1/100 000 and 1/1 000 000 are 17, 1.7 and 0.17µg.m^{-3}, respectively.		World Health Organisation (2010)	The risk estimates are based on human health risk. However, it is noted that the current Defra national air quality objectives for benzene for England and Wales is an annual mean of 5µg.m^{-3}, based on the European (EU) ambient air quality directive 2008/50/EC (EU, 2008), (Defra, 2010).	The International Agency for Research on Cancer has classified benzene as carcinogenic to humans (Group 1). Benzene causes acute myeloid leukaemia in adults. Positive associations have been observed for non-Hodgkin lymphoma, chronic lymphoid leukaemia, multiple myeloma, chronic myeloid leukaemia, acute myeloid leukaemia in children and cancer of the lung. (IARC, 2018a).
D-Limonene (5989-27-5)	90,000 (30min)	9000 (1 day)	EPHECT (Trantallidi et al., 2015)	Critical Exposure limit (CEL) inhalation exposure to key and emerging indoor air pollutants emitted during household use of selected consumer products	As for α-Pinene above
Formaldehyde (50-00-0)	100 (30min)	10 (1yr)	World Health Organisation (2010). ATSDR MRL (1999)	World Health Organisation guidelines valid for short term exposure. ATSDR value of 10 µg/m^3 suggested as the long-term health-based guideline value which accounts for the potential for child susceptibility.	Sensory irritation of the eyes, nose and throat, together with exposure-dependent discomfort, lachrymation, sneezing, coughing, nausea and dyspnoea. Human carcinogen -long-term exposure linked to nasal cancer.[1]
Naphthalene (91-20-3)	-	3.0$^+$ (1yr)	Agency for Toxic Substances & disease Registry (2005), USA	Value also selected by the Flemish Government (2018) There is no proposed guideline for short term exposure due to the lack of scientific evidence.	Haemolytic anaemia in humans at high doses. Respiratory tract lesions including carcinogenicity reported in long-term animal studies. [1,3]

Table 1 contd. Indoor air quality guidelines for selected VOCs in the UK (µg.m^{-3})

VOCs	Limit Values in µg.m^{-3}		Source Document	Reasoning for choice	Potential Health impacts
	Short Term	Long Term			
Styrene (100-42-5)	-	850 (1y)^	Health Canada (2018)	Most recent appraisal of evidence	Sensory irritation of the eyes, nose and throat. High concentrations- headache, nausea, vomiting, weakness, tiredness, dizziness, mild irritation to skin. Long-term exposure has been reported to cause neurological effects in humans including changes in hearing, balance, colour vision and psychological performance.
Tetrachloroethylene (127-18-4)	-	40 (1day)	US EPA (2012) and Health Canada (2018)	Most recent appraisals of evidence	Effects in the kidney indicative of early renal disease and neurotoxicity (visual and autonomic disturbances)[1,3] Evidence of carcinogenicity in animals. Limited evidence for carcinogenicity in humans (positive associations have been observed for bladder cancer)
Toluene (108-88-3)	15,000 (8h)	2,300 (1 day average)	Health Canada (2018)	Most recent appraisal of evidence, specifically the dose response relationship.	Eye, nose and throat irritation, headaches, dizziness and feelings of intoxication following short-term exposure. Neurological effects including reduced scores in tests of short-term memory, attention and concentration following long-term exposure[2]
Trichloroethylene* (71-01-06)	No safe level of exposure can be recommended. Based on continuous exposure to 1 µg.m-3 from birth to age 70 the estimated lifetime unit risk of kidney cancer (adjusted for other cancers) is 4.8 x 10-6. The concentrations of airborne trichloroethylene associated with an excess lifetime cancer risk of 1/10 000, 1/100 000 and 1/1 000 000 are 21, 2.1 and 0.21 µg.m-3, respectively. respectively.		World Health Organisation (2010)	This value is based on human data for kidney cancer, which has also been adjusted for other cancers.	The International Agency for Research on Cancer has classified trichloroethylene as carcinogenic to humans (Group 1). Trichloroethylene causes cancer of the kidney. A positive association observed for non-Hodgkin lymphoma and liver cancer. It is assumed that trichloroethylene is genotoxic (IARC, 2018b)
Xylenes-mixture (1330-20-7)	-	100 (1y)^	Health Canada (2018)	Most recently derived and most precautionary value.	Irritation to the nose, throat and lungs. Severe inhalation exposure can cause dizziness, headache, confusion, heart problems, liver and kidney damage and coma[2]

*No safe level of exposure can be recommended. The concentrations shown are associated with an excess lifetime risk of 1/1,000,000 and are applicable to both long and short-term exposures.
+We are aware of new data that indicates that effects may occur at lower doses; however, this new data has not yet been evaluated by an authoritative body.
^ Health Canada uses screening values for some species - Indoor Air Reference Levels (IARL). These are used to assess possible risk. They are associated with acceptable levels of risk after long-term exposure (over several months or years) for each specific VOC. Due to uncertainties in derivation; these have simply been labelled as annual. In these cases, no separate short-term exposure limit has been stated.

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INFORME COMISIÓN ESPECIAL INVESTIGADORA SOBRE CAUSAS DE ALTA CONTAMINACIÓN AMBIENTAL, ESPECIALMENTE EN CONCÓN, QUINTERO Y PUCHUNCAVÍ, Y DE RESPONSABILIDADES EN EJECUCIÓN DEL PLAN DE DESCONTAMINACIÓN.

HONORABLE CÁMARA:

La Comisión Especial Investigadora individualizada en el epígrafe, cumple con emitir su informe -según la competencia que le fuera asignada por acuerdo de la Cámara de Diputados-, planteando las conclusiones y recomendaciones que al final se consignan.

I.- COMPETENCIA DE LA COMISIÓN AL TENOR DEL ACUERDO DE LA CÁMARA QUE ORDENÓ SU CREACIÓN.

A) CREACIÓN DE LA COMISIÓN.

Por oficio N° 14.190, de 4 de septiembre de 2018, de la Secretaría General, se informó que la Cámara de Diputados, en sesión de la misma fecha y en virtud de lo dispuesto en los artículos 52, N° 1, letra c) de la Constitución Política de la República; 53 de la Ley Orgánica Constitucional del Congreso Nacional, y 297 y siguientes del Reglamento de la Corporación, dio su aprobación a la solicitud de 64 señoras diputadas y señores diputados, para que la Comisión se constituyera en calidad de investigadora a fin de analizar, indagar y determinar las causas de la alta contaminación ambiental, en las denominadas “zonas de sacrificio”, especialmente en Concón, Quintero y Puchuncaví, y los actos de las autoridades del Gobierno, para prevenir, regular, fiscalizar y remediar la situación, y para controlar los efectos sobre la salud de las poblaciones aledañas a dichas zonas.

En el ejercicio de su cometido, la Comisión deberá “recabar antecedentes sobre las causas de la alta contaminación ambiental en las denominadas “zonas de sacrificio” y, en particular, en la zona de Quintero – Puchuncaví, con motivo de la última alerta surgida por la intoxicación que afectó a más de 200 personas, así como también sobre los actos de las autoridades del Gobierno, especialmente de los Ministerios de Medio Ambiente, y de Salud, y de las secretarias regionales ministeriales de ambas carteras, para prevenir, regular, fiscalizar y remediar la situación, y para controlar los efectos sobre la salud de las poblaciones aledañas a dichas zonas.”.

Cabe hacer presente que previamente la Cámara de Diputados, mediante oficio N° 14. 119, de fecha 7 de agosto de 2018, acordó la creación de una Comisión Investigadora con similar objeto de Investigación.

En virtud de lo anterior y motivada en un acuerdo de los Comités Parlamentarios, la Sala, en sesión 66ª, celebrada el 4 de septiembre de 2018, acordó fusionar esta nueva Comisión con la Comisión Especial investigadora de las causas de la alta contaminación ambiental, especialmente en Concón, Quintero y Puchuncaví, y de las responsabilidades en la ejecución del Plan de Descontaminación.

Las Comisiones Investigadoras, así fusionadas, deberán rendir su informe en un plazo no superior a noventa días y para el desempeño de su cargo podrá constituirse en cualquier lugar del territorio nacional.

Por oficio N° 14. 431, de 2 de enero de 2019, se comunicó que la H. Sala, accedió a lo solicitado por la Comisión en orden a ampliar el plazo para cumplir con su mandato en 14 días, más los 15 días como máximo para la redacción de las conclusiones y proposiciones.

A) INTEGRACIÓN Y PRESIDENCIA DE LA COMISIÓN

Mediante oficio N° 14.193, de 5 de septiembre de 2018, la Corporación acordó integrar la Comisión con las y los siguientes diputados:

Doña Camila Flores Oporto.
Doña María José Hoffmann Opazo.
Don Diego Ibáñez Cotroneo.
Don Pablo Kast Sommerhoff.
Don Amaro Labra Sepúlveda.
Don Andrés Longton Herrera.
Doña Carolina Marzán Pinto.
Don Luis Pardo Sáinz.
Don Patricio Rosas Barrientos.
Don Alejandra Sepúlveda Órbenes.
Don Marcelo Schilling Rodríguez.
Don Osvaldo Urrutia Soto.
Don Daniel Verdessi Belemm.

Durante la sesión constitutiva de esta Comisión Especial Investigadora, celebrada el día 5 de septiembre de 2018, se eligió, por unanimidad, como Presidente de ella, al diputado señor Diego Ibáñez Cotroneo.

Posteriormente por oficio N° 14.209, de 11 de septiembre de 2018, la Secretaría de la Cámara de Diputados comunicó el reemplazo permanente de la diputada Alejandra Sepúlveda Órbenes por el diputado René Saffirio Espinoza.

II.-ANTECEDENTES GENERALES.

El desarrollo industrial de la localidad de Ventanas, ubicado en la comuna de Puchuncaví, Región de Valparaíso, tiene una historia de larga data, pues fue instalado hace casi 60 años, siendo inaugurado en el año 1961 con el objetivo de generar un polo de desarrollo industrial en la Región[1]

Sin embargo su historia se remonta a fines de la década del 50, con la entrada en funcionamiento en 1958 de CHILECTRA, que posteriormente pasa a llamarse AES GENER; periodo, en que, además, se inicia la construcción de una fundición por la Empresa Nacional de Minería, la que fue inaugurada en 1964, y ese mismo año entra en funcionamiento VENTANAS I, central termoeléctrica con una potencia instalada de 115.000 Kw, diseñada con técnicas modernas, para esa época, que le permiten funcionar con carboncillo y en casos de emergencia con petróleo. Más adelante, la refinería electrolítica para el tratamiento de metales como el cobre, oro y plata, propiedad de la Empresa Nacional de Minería (ENAMI), de propiedad

[1] Universidad Diego Portales, 2012.

estatal. También se erigió una central termoeléctrica Ventanas 1, en el año 1964 operada por Chilectra Generación (Chilgener). Más adelante se construyeron las de Ventanas 2 en 1977, Nueva Ventanas en 2006 y la Central Campiche en 2013, operadas hoy en día por la empresa AES Gener, continuadora legal de la empresa pública, luego de su privatización. La potencia completa del complejo termoeléctrico alcanza los 885 MW, siendo el más grande de Chile de este tipo[2].

Estas instalaciones fueron emplazadas en la zona en razón de su disponibilidad de agua, la cercanía con los puertos de Quintero y Valparaíso para el embarque de sus productos y la ubicación de los centros y proyectos mineros de esa época. Nace así el complejo industrial Ventanas que fue inaugurado el 12 de febrero de 1961, el que, según expresaba El Mercurio de Valparaíso de la época, constituía una "llanura abierta a distancia aproximada de 14 kilómetros de los cerros y expuesta a los vientos del mar, no ofrece peligros de contaminación por gases atmosféricos".

No obstante, su funcionamiento ha impactado ambientalmente la bahía ante lo cual las compañías y la autoridad han adoptado diversas medidas de control de emisiones y de mitigación.

Sin embargo, existen otras comunas en Chile que viven situaciones similares, es decir sectores geográficos de alta concentración industrial, en los que se ha priorizado el establecimiento de polos industriales por sobre el bienestar de las personas y el ambiente, a ello se suma el malestar de sus habitantes que luchan día a día para exigir cambios radicales y así mejorar sus condiciones de vida. A estos lugares se les ha denominado "zonas de sacrificio",

Es así como de las 28 termoeléctricas a carbón que operan en el país, 27 se concentran en solo cinco comunas: **Tocopilla**, que alberga 7 centrales: 5 de Engie y 2 de AES Gener; **Mejillones**, con 8 termoeléctricas: 4 de Engie y 4 de AES Gener; **Huasco,** con 5 centrales, todas de AES Gener; **Puchuncaví** alberga 5 y también todas son de AES Gener; y **Coronel** en que hay 3, 2 de Enel y una de Colbún.

De acuerdo a un informe de Chile Sustentable, las 28 termoeléctricas son responsables del 91% de las emisiones totales de dióxido de carbono (CO2), el 88% de la totalidad de material particulado (MP), el 97% de las emisiones totales de SO2 y el 91% de las emisiones totales de óxidos de nitrógeno (NOx).

Respecto de la concentración de los contaminantes señalados por zona, la relación en 2017 fue la siguiente: el 32% del total de las emisiones del parque carbonero se aglutinó en Mejillones, 22% en Puchuncaví, 17% en Tocopilla, 15% en Huasco, y 11% en Coronel.

A continuación se desarrollan los temas más relevantes analizados por la Comisión, en relación con las causas de la alta contaminación ambiental en las "zonas de sacrificio" y, en particular, en la zona de Quintero – Puchuncaví, junto con los actos de las autoridades para prevenir, regular, fiscalizar y remediar la situación y los efectos sobre la salud de la población. Asimismo se analizó e investigó las responsabilidades en la ejecución del fallido plan de descontaminación para comunas de Concón, Quintero y Puchuncaví.

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[2] Disponible en: http://proyectoconflictos.ulagos.cl/wp-content/uploads/2016/07/Complejo-Termoel%C3%A9ctrico-Ventanas.pdf.

A) INCIDENTES AMBIENTALES EN LA BAHÍA DE QUINTERO.

El 20 de agosto del 2018 se inició una serie de situaciones de emergencia que hasta el momento se mantienen sin respuestas claras por parte de la autoridad en cuanto a la imputación certera de responsabilidades. Entre el día lunes 20 y martes 21 de agosto, se registraron cerca de 70 casos de niños, niñas y adolescentes, en su mayoría, que llegaron al hospital Adriana Cousiño de Quintero con síntomas de intoxicación, lo cual provocó la evacuación de diversos colegios ubicados en la comuna de Quintero y la suspensión de las clases para el día 22 y 23 de agosto, tanto para establecimientos educacionales como para jardines infantiles, municipalizados y subvencionados particulares.

Con fecha 23 de agosto la Oficina Nacional de Emergencias (ONEMI), del Ministerio del Interior y Seguridad Pública, evacuó informe de incidente o emergencia, por medio del cual comunicó la decisión de declarar alerta amarilla en las comunas de Quintero y Puchuncaví, fundado en el informe técnico N°726 del mismo organismo, en el que se constata la presencia de Metilcloroformo, Nitrobenceno y Tolueno en el ambiente de las comunas de Quintero y Puchuncaví, informando la intoxicación por contaminación atmosférica de 133 personas en la zona. Asimismo, las municipalidades de las comunas afectadas, en coordinación con la Secretaría Regional Ministerial de Educación, determinaron la suspensión de la jornada escolar para el día viernes 24 de agosto, para todos los establecimientos educacionales de la zona.

Tras diez días de paralización de las actividades académicas y ocho días de alerta amarilla, el sábado 1 de septiembre se levantó la alerta que se había declarado en la zona, ordenando la reanudación de clases para el martes 4 de septiembre. Se indicó como fundamento que en los últimos cuatro días había disminuido drásticamente la cantidad de personas intoxicadas y que las mediciones realizadas por los equipos de monitoreo, habían bajado a niveles no riesgosos para la vida y salud de la comunidad.

A pesar de los resultados arrojados por los centros de monitoreos, en el primer día de reanudación de clases, nuevamente se presentaron alrededor de 70 alumnos con síntomas de intoxicación, náuseas, cefaleas y vómitos, constituyéndose en el tercer episodio de intoxicación en menos de dos semanas. Las autoridades, reconocieron que los instrumentos no detectaron las emanaciones y que ello dificulta la búsqueda de los responsables, al existir más de 15 industrias emplazadas en la zona.

El último episodio descrito, llevó a que el Comité Operativo de Emergencia de la Región de Valparaíso, declarara una nueva alerta amarilla, suspendiendo nuevamente las jornadas escolares, el martes 20 de septiembre se levanta la alerta amarilla.

Posteriormente se plantea que el 24 de septiembre ocurrió un cuarto hecho, después de haber dado término a la alerta amarilla y tras decretar una disminución de las actividades de varias de las empresas sospechosas de causar la crisis sanitaria y se detiene en el efecto de una serie de sustancias.

El 24 de septiembre se decreta Alerta Sanitaria para las comunas de Quintero y Puchuncaví, para enfrentar la emergencia de salud que afectaba a esta zona desde el martes 21 de agosto. Justo cuando se informaban estas medidas, una

decena de alumnos de tres establecimientos llegaron hasta el Hospital de Quintero, donde se les diagnosticó “intoxicación por gas“. A partir de la dictación de este decreto se toman las primeras medidas que logran reducir los episodios de contaminación.

El 28 de diciembre como lo dispuso el decreto de Alerta Sanitaria se ingresó a la Contraloría General de la República del Plan de Prevención y Descontaminación Atmosférica para las comunas de Concón, Quintero y Puchuncaví y la nueva norma de calidad primaria de dióxido de azufre.

B) OTRAS ZONAS DE SACRIFICIO.

Las zonas de sacrificio son sectores geográficos de alta concentración industrial, en los que se ha priorizado el establecimiento de polos industriales, por sobre el bienestar de las personas y el ambiente. Este concepto fue acuñado por la Agencia de Protección Ambiental de Estados Unidos (EPA). Las zonas de sacrificio son mayormente lugares de bajos ingresos, en los cuales se han instalado industrias declarando intenciones de desarrollo, además de mejoras en las condiciones de trabajo y vida para sus habitantes. Sin embargo, sus habitantes alegan que la contaminación ha degradado su salud y bienestar, además de deteriorar ecosistemas marinos y terrestres necesarios para su bienestar y desarrollo económico local.

En Chile este término se comienza a conocer luego de la movilización de la comunidad de la bahía de Quintero, después del episodio de contaminación que afectó a alumnos y profesores de la escuela “La Greda”, “Alonso Quintero” y “Francia” en 2011. Este episodio reabrió el debate respecto a la situación de contaminación en la zona de Puchuncaví.

Posterior se acuña el concepto de “zonas de sacrificio”. Si bien este concepto no tiene una validación oficial, diversas organizaciones en todo el mundo ya lo han comenzado a utilizar, siendo definido por el Instituto de Derechos Humanos (INDH) como una “situación de injusticia ambiental evidente, por cuanto los beneficios que genera [una industria] se reparten.[3]

En nuestro país el INDH y las organizaciones de la sociedad civil han catalogado a seis comunas como “zonas de sacrificio”.

3 Disponible en https://pras.mma.gob.cl/wp-content/uploads/2018/02/PRAS-Coronel-27022018.pdf

TOCOPILLA

Comuna ubicada en la Región de Antofagasta, en el norte del país. Se encuentra a una distancia de 168 km de Antofagasta, la capital regional. Tiene una superficie de 4.039 km2. Limita al norte con la comuna de Iquique, y al sur con la comuna de Mejillones, al este con la comuna de María Elena y al oeste con el Océano Pacífico, con más de 145 km de costa.

Su principal centro poblado es la ciudad de Tocopilla, capital comunal.

De acuerdo al INE (2015), la comuna tiene una población de 26.931 habitantes.

El equipamiento de la comuna para el sector salud y educación está compuesto para el sector salud con 1 hospital de los 5 existentes en la región. No posee ningún otro tipo de establecimiento de salud. En el sector educación, la comuna posee 11 establecimientos, de los 233 que hay que la región.

Desarrollo económico: Por su característica costera, Tocopilla tiene un puerto donde ha desarrollado su economía en base a éste debido a la gran actividad minera que se desarrolla en la región. De acuerdo al actual Plan de Desarrollo Comunal, su desarrollo económico está basado en la generación eléctrica (que suministra aproximadamente el 50% del consumo regional) y la actividad portuaria, esta última de gran importancia a nivel regional y en menor medida, a la actividad pesquera. La industria minera en la región necesita de la conectividad para la exportación/importación de productos necesarios y de energía para el desarrollo de la minería. Tocopilla es un gran soporte en este aspecto, ya que posee el puerto y termoeléctricas. Las otras industrias existentes en la comuna son una planta productora de cobre, una industria pesquera, un puerto mecanizado de salitre y de descarga de carbón, y un terminal de ferrocarril salitrero. Estas industrias, especialmente las termoeléctricas generan algunos puestos de trabajo en la comuna.

Impactos detectados productos de la actividad industrial: Tocopilla concentra industrias contaminantes que repiten patrones en cuanto a emisión de contaminantes atmosféricos, producto de las termoeléctricas, como anhídrido sulfuroso; material particulado provenientes del petcoke (combustible compuesto por la mezcla de petróleo refinado con carbón) y carbón; metales pesados como níquel y vanadio. La salud de las personas también es una preocupación producto de la constante exposición a contaminantes que implica este centro industrial, especialmente asociados a enfermedades respiratorias/pulmonares por la presencia de malos olores, emisión de gases producto de las termoeléctricas y actividades que emiten contaminantes microscópicos al aire, como el material particulado. La contaminación presente en la comuna proviene principalmente de la concentración de estas actividades industriales. La contaminación es apreciable en las playas, como en la ciudad (hollín, malos olores), lo que lo hace absolutamente incompatible con la actividad turística.

MEJILLONES

Comuna ubicada en el norte de Chile, en la región de Antofagasta. Se encuentra a 65 kilómetros al norte de la capital regional, la ciudad de Antofagasta. Con una superficie de 3.803,9 km2, limita al norte con la comuna de Tocopilla; al Este con la comuna de María Elena y Sierra Gorda; al sur con la comuna de Antofagasta. Su límite oeste es el Océano Pacifico. Esta comuna costera perteneció a Bolivia y tras la Guerra del Pacífico pasó a ser parte de Chile.

El principal centro urbano de esta comuna es la ciudad de Mejillones.
De acuerdo a INE (2015). Cuenta con una población de 26.931 habitantes.

Equipamiento: En el sector salud cuenta sólo con un centro de salud (un hospital) de los cinco que se encuentran en la región. En sector educación, tiene 6 establecimientos (4 establecimientos municipales y 2 particulares).

Desarrollo económico: La pujante industria salitrera reafirmó la vocación de conectividad de la ciudad por poseer un puerto, espacio que facilitó la exportación de salitre, y con ello un desarrollo a partir de esta industria. Desde ese tiempo hasta hoy Mejillones ha acentuado la actividad portuaria en torno a la ciudad, como el desarrollo de cierto tipo de industrias que necesitan de esta conectividad. La industrialización tuvo un auge a partir de la década de los 90, como una alternativa a la crisis pesquera. Se instalan termoeléctricas, fábrica de explosivos Enaex, Interacid, además de Cementos Polpaico, ácido sulfúrico, minería, concentrado de plomo, industria portuaria y transporte ferroviario constituyen el eje del desarrollo industrial de esta comuna.

Impactos detectados productos de la actividad industrial: Aun cuando se instalaron los Fertilizantes, que generaban contaminación, los impactos no eran tan evidentes. Hoy producto de la concentración de industrias, los impactos negativos la población los aprecia día a día, especialmente en la contaminación del aire producto de la actividad industrial que generan las empresas pesqueras (además del mal olor), de ácido sulfúrico, de explosivos, cemento, y energía eléctrica provenientes de centrales térmicas. Hay evidencia de metales pesados en el fondo marino, producto de operaciones portuarias (embarques y descargas de productos). A pesar de las 10 unidades de generación eléctrica existente, además de todas las otras industrias altamente contaminantes, Mejillones hoy no está contemplada legalmente como Zona Latente (mucho menos Saturada) de contaminación, y carece por ello, de planes de descontaminación.

HUASCO

La comuna de Huasco está conformada por dieciocho localidades entre ellas Huasco, Huasco Bajo, Canto de Agua y Carrizal Bajo. Es administrada por la Ilustre Municipalidad de Huasco y limita al norte con la comuna de Copiapó, al sur con la comuna de Freirina, al este con las comunas de Freirina y Vallenar; y al oeste con el Océano Pacífico.

La ciudad de Huasco, capital comunal, es un balneario cercano a la desembocadura del río Huasco, que destaca por sus bellas postales y por conservar aún su tranquila vida. Posee una infraestructura portuaria considerada la más importante de la Región de Atacama y dista 46 km de Vallenar, capital provincial; y 191 km de Copiapó, capital regional

Principal centro urbano: La ciudad de Huasco es el principal centro urbano de la comuna. Población: Se estima que la población de la Comuna de Huasco asciende a 9.737 habitantes (INE 2015).

Equipamiento: En cuanto al sector salud y educación, esta comuna cuenta con s centros de salud de los 40 que hay en la región (1 hospital, 3 postas rurales y 1 centro de salud ambulatorio). En cuanto a equipamiento educacional, esta comuna tiene 10 establecimientos de los 181 que hay en la región.

Desarrollo económico: Emplazada en la costa, el desarrollo portuario de Huasco data desde el año 1600 en el sector llamado "puerto viejo" de donde se extraen minerales, especialmente cobre. El auge del salitre abrió otro espacio de exportación para abastecer a las salitreras, como productos agrícolas a lo largo del valle del Huasco (aceitunas, vinos o vacunos). El desarrollo minero en el norte de Chile permitió que el desarrollo económico de Huasco fuera en torno a la actividad agrícola pero también en base a la actividad portuaria de embarque. Hoy su economía se ha consolidado en torno al puerto, especialmente como exportador de pequeña y mediana minería de hierro de la región. La instalación de termoeléctricas también ha generado actividad económica y en menor importancia la agricultura. La actividad turística o pesquera artesanal también se genera en la comuna, pero en otras localidades corno Carrizal. Hoy Huasco tiene instalaciones termoeléctricas, una planta de pellets, actividad portuaria que ha generado un foco de contaminación proveniente de estas actividades, con mucha evidencia en el aire, playas, y casco urbano.

Impactos detectados productos de la actividad industrial: La actividad industrial que se ha desarrollado en torno a la actividad portuaria no dista de la contaminación procedente de ésta. El Plan de Desarrollo Comunal (Pladeco) menciona que existen presiones que afectan los componentes ambientales de la zona, éstas se pueden catalogar como industrias altamente contaminantes cuales ponen en riesgo la calidad de vida y el desempeño productivo de sus habitantes. La plata de pellets de hierro es de la Compañía Minera del Pacífico (CMP) data de 1978 y contiene alta concentración de contaminantes, como fósforo y azufre. Esta planta realiza muchos procesos químicos para extraer el hierro, genera residuos al igual que la termoeléctrica (material particulado negro) que, son levantados por el viento y contaminan el aire, la ciudad y a sus habitantes por no tener suficiente protección de acopio. El depósito de este material está afectando gravemente a las plantas, especialmente a la producción agrícola. La termoeléctrica utiliza petcoke (combustible compuesto por la mezcla de petróleo refinado con carbón) y con esto produce emisión de anhídrido sulfuroso, dióxido de azufre, material particulado respirable fino (PM 10 y el PM 2,5), metales pesados, corno níquel y vanadio, entre otros.

CORONEL

Ubicada en el centro-sur de Chile, en la Región del Bio Bio. Se encuentra a 30 kilómetros al sur de la capital regional, la ciudad de Concepción. Con una superficie de 279 km2, limita la norte con la comuna de San Pedro de la Paz, al este con el río Bio Bio (límite natural con /a comuna de Concepción y Hualqui); al sur con las comunas de Lota y Santa Juana. Al Oeste limita con el Océano Pacifico.

Su principal centro urbano es la ciudad de Coronel, capital comunal.

De acuerdo al INE (2015) cuenta con una población de 111.455 habitantes.

Equipamiento: En el sector salud sólo con 11 centros de atención de los 353 que existen en la región (1 hospital, 7 centros de salud ambulatorios y 3 postas rurales). Para el sector educación, tiene 63 establecimientos de los 1.584 que hay en la región.

Desarrollo económico: En términos económicos, Coronel fue un punto importante para el desarrollo minero que se generó en la zona a partir de las minas de carbón (junto con Lota) aproximadamente del año 1847, fecha de su fundación como comuna. El importante rol que tenía el puerto de Coronel duró hasta el año

1990, fecha en las minas de carbón se cerraron casi en su totalidad. En este periodo comienza el incentivo para la instalación de ciertas industrias con la creación de "parques industriales" para contrarrestar la crisis económica y pérdidas de fuentes laborales que dejó el cierre de las minas.

Hoy su localización en el centro-sur del país, adosado a su puerto, la comuna se ha consolidado en aspectos industriales portuarios, además de la instalación de termoeléctricas y el desarrollo de sectores productivos, como el forestal y pesquero en menor medida. La actividad pesquera está presentando una importante reducción dada la sobreexplotación de los recursos, además de la contaminación de las aguas de la bahía.

Impactos detectados productos de la actividad industrial: La alta concentración de industrias contaminantes ha generado una mala calidad del aire con evidentes índices de contaminantes provenientes de las termoeléctricas y sus procesos industriales. Se ha declarado la comuna como "zona latente" por ser parte del Gran Concepción, además de la contaminación producida por la utilización de calefacción con leña (saturación de Material Particulado Respirable PM10). Ante la denuncia ciudadana de que muchas industrias generan emisiones atmosféricas por procesos de combustión irregulares, se suma que la Bahía de Coronel es uno de uno de los principales núcleos industriales pesqueros del país, generando externalidades negativas en la ciudad, ya sea por los malos olores derivados de faenas con materia prima en descomposición y la emisión de gases por los propios procesos industriales. Por otro lado, la Central Termoeléctrica Bocamina (de propiedad de Endesa Chile S.A.), data desde el año 1970, por lo que no cumple con los estándares ambientales mínimos que hoy se exigen a este tipo de instalaciones. De todas formas, de las 4 unidades termoeléctricas que hay en la comuna, solo una cuenta con RCA aprobada; las otras no presentaron ningún tipo de estudio o declaración de impacto ambiental.

C) PARQUE INDUSTRIAL VENTANAS.

Como anteriormente se expuso, las comunas de Concón, Quintero y Puchuncaví, han sido denominadas como “zonas de sacrificio”[4], debido a que el Estado ha permitido la instalación de un complejo industrial altamente contaminante generando un impacto tal en el territorio, que el aire, el suelo y las aguas han quedado dañadas por la depredación industrial, afectando al medio ambiente, la vida de las comunidades cercanas y el ejercicio de sus derechos fundamentales.

Como toda zona de sacrificio, estas localidades han sido abatidas por una serie de eventos, entre los que se destaca el derrame de más de 38 mil litros de crudo al mar, en el año 2014[5], por una mala conexión de un buque con la terminal de una de las empresas del complejo, hechos que se reiteraron en el año 2015 y en mayo del 2016. Aun así, el fenómeno es mayor, pues de acuerdo a información de la Dirección General del Territorio Marítimo y Marina Mercante (DIRECTEMAR), desde el año 2000 al 2013, esta zona ha sufrido el 9,6% de todos los derrames registrados en Chile de manera oficial[6]. A ello se suman los diversos varamientos de carbón que

[4] Para mayor información ver https://www.indh.cl/wp-content/uploads/2014/12/Territorios-y-derechos-humanos-INDH-2014.pdf Consultado el 11 de diciembre de 2018.
[5] Disponible en: http://www2.latercera.com/noticia/los-derrames-de-petroleo-que-han-marcado-la-costa-de-quintero/. Consultado el 9 de septiembre de 2018.
[6] 24Contaminación de zona industrial de Ventanas, comuna de Quintero y Puchuncaví Biblioteca del Congreso Nacional Enrique Vivanco Font en colaboración con Verónica de la Paz y Rafael Torres, Departamento de Estudios Extensión y Publicaciones. Asesoría Técnica Parlamentaria, 2014.

se han presenciado en las costas de Ventanas, llegando a alcanzar cerca de 300 sucesos desde el año 2008 a agosto de 2018, el último de ellos en agosto de 2018[7].

La salud de las personas que viven en los alrededores del cordón industrial, se ha visto fuertemente afectada en diversas ocasiones. En marzo del año 2011 una falla en la división Ventanas de la empresa Codelco generó una nube tóxica que dejó a niños y niñas de la Escuela Básica La Greda, ubicada en Puchuncaví, con diversos síntomas de intoxicación.

Tales hechos se volvieron a reiterar en noviembre de ese mismo año, registrándose 31 niños y niñas y 9 adultos.26 A raíz de este suceso, la escuela fue clausurada y reubicada en otro lugar dentro de la comuna[8]. Sin embargo, en septiembre del 2015, hubo una nueva intoxicación de 40 alumnos del nuevo establecimiento, debiendo ser cerrado[9].

En el año 2015 el Ministerio de Medio Ambiente declaró, a las comunas de Concón, Quintero y Puchuncaví, como zona saturada por material particulado fino respirable MP25 tanto por concentración anual y latente como concentración diaria, y zona latente por material particulado respirable MP10, como concentración anual[10]. Tal declaración conlleva a que el Estado de Chile deba cumplir con el imperativo legal establecido en el artículo 43 de la ley 19.300 de Bases Generales del Medio Ambiente y elaborar un plan de descontaminación o de prevención, respectivamente, para las comunas que son parte de la declaración de saturación o latencia.

Cabe hacer presente que en la zona, existe sólo un plan de descontaminación aprobado en 1992 que obliga solamente a las empresas CODELCO y AES GENER a establecer una red de monitoreo de sus emisiones (que es la única existente en la zona y que hasta antes de estos últimos episodios de contaminación, era operada por las mismas empresas que contaminan) y a cumplir normas de calidad del aire para material particulado 10 (MP10) y Anhídrido Sulfuroso (SO_2)[11].

Debido a la falta de regulación para las demás empresas, el Estado, a través del Ministerio del Medio Ambiente, elaboró un Plan de Descontaminación global para las comunas de Concón, Quintero y Puchuncaví, el cual fue rechazado por la Contraloría General de la República en diciembre del año 2017 por no ajustarse a derecho. Esto porque "[l]as medidas dispuestas para las aludidas fuentes puntuales, diseñadas sobre la base de esos niveles que son mayores a la real contribución de emisiones por parte de ellas, no se traducen en una efectiva reducción de los contaminantes de que se trata, por lo que el presente instrumento de gestión ambiental no cumple con la finalidad que la normativa le asigna"[12]. Hasta el día de hoy no existe un instrumento vigente de descontaminación para esta zona.

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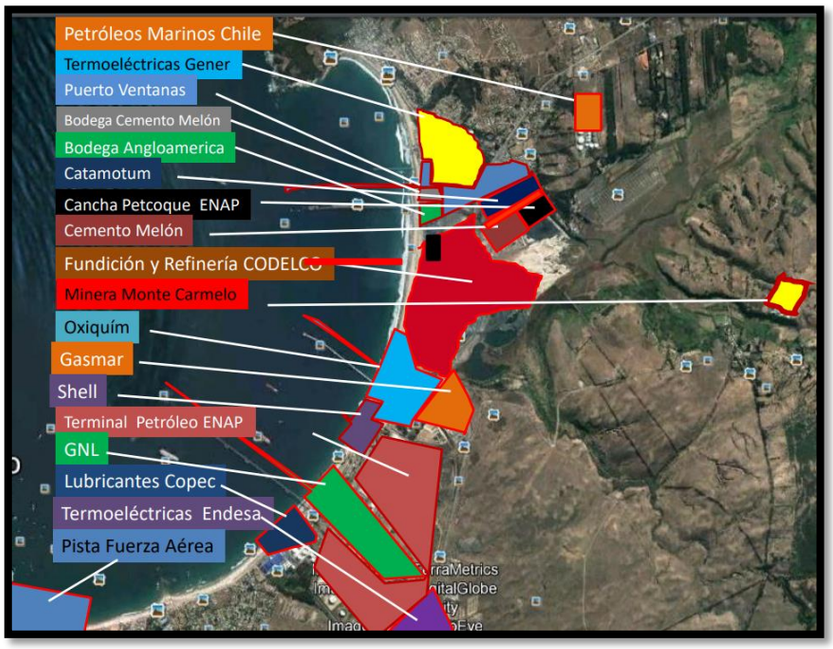
[7] Disponible en:http://www.terram.cl/2017/11/varamientos-de-carbon-en-ventanas-una-situacion-de-abandono/ Consultado el 9 de septiembre de 2018.
[8] Disponible en: http://www.elmostrador.cl/noticias/pais/2011/11/24/emanaciones-vuelven-a-intoxicar-a-estudiantes-y-profesores-de-la-escuela-la-greda/ Consultado el 8 de septiembre de 2018.
[9] Disponible en: http://www.soychile.cl/Valparaiso/Sociedad/2015/09/14/346123/Una-veintena-de-ninos-se-intoxico-en-la-escuela-La-Greda-de-Puchuncavi.aspx. Consultado el 21 de septiembre de 2018.
[10] Decreto 10 del Ministerio de Medio Ambiente del año 2015, publicado en el Diario Oficial con fecha 9 de junio de 2015. Disponible en: http://portal.mma.gob.cl/transparencia/mma/doc/DS-10_Declara-Zona-Saturada-Lantente-Concon-Quintero-Puchuncavi.pdf.
[11] Universidad Diego Portales, 2012.
[12] Sesión 9ª celebrada en 5 de noviembre de 2018, dichos del Contralor General de la República.

A continuación, se detallan las empresas más destacadas que desarrollan sus actividades en la zona, tal como se aprecia en lámina.



Actualmente, el parque industrial está conformado, entre otras, por alguna de las siguientes empresas:

1.- CATAMUTÚN ENERGÍA S.A.

Es una empresa dividida en dos áreas de trabajo: división carbón y división vapor.

La división carbón está dedicada a la importación y distribución de carbón térmico, transporte, manejo de canchas y servicios relacionados, asesorías en proyectos térmicos a carbón, operación de equipos, logística y manejo, control de emisiones.

En Ventanas tiene uno de los terminales de importación de carbón, donde se puede descargar naves de 40 a 55 mil toneladas a ritmos de 8 a 15 mil toneladas por día. Su capacidad de almacenamiento es del orden de 150 mil toneladas en cada terminal -también cuenta con un terminal de importación en Penco-.

Además de la importación de carbón, se dedica al cribado de carbón produciendo diferentes granulometrías para uso en calderas de parrillas, al transporte de carbón vía camiones y ferrocarril.

2.- CEMENTO MELÓN.

Esta empresa ha construido dentro de los recintos portuarios de Puerto de Ventanas, una bodega tipo domo para el almacenamiento de clinker-bauxita, compuestos empleados para la elaboración del cemento.

El producto es recepcionado desde los barcos en el sitio Nº 5, mediante una tolva que descarga el producto sobre una correa transportadora para luego enviarla hasta otra tolva de recepción ubicada en la parte superior del domo.

Una vez en el domo, la carga es transferida a una cinta transportadora y ésta, a su vez, envía el producto a una tolva de despacho común para la carga de tren y camiones con este material. Estas tres tolvas cuentan con equipo de control del tipo filtro de mangas.

3.- CODELCO DIVISIÓN VENTANAS.

Es una fundición y refinería de cobre que produce cátodos de cobre, lingotes de oro y granalla de plata. La capacidad de fusión de concentrados de Ventanas fue de 445 mil toneladas métricas secas para el año 2006. La producción el año 2006 alcanzó a 376.005 toneladas métricas de cobre electrolítico.

Asimismo, por el procesamiento de los barros anódicos de la refinería en la planta de metales nobles, se produjeron 150.952 kilos de plata y 5.649 kilos de oro; y la planta de ácido produjo 351.537 toneladas de ácido sulfúrico.

4.- COMPLEJO TERMOELÉCTRICO AES GENER S.A. – CENTRAL VENTANAS

Empresa generadora de energía, constituida como la segunda más grande en capacidad instalada del país18. Cuenta con un complejo de 4 centrales termoeléctricas que opera en base a la combustión de carbón, ubicado en la comuna de Puchuncaví, en la Bahía de Quinteros, con una capacidad total de 884 MW.

Cada unidad está conectada a un precipitador electroestático de tres campos que retiene las partículas suspendidas en el flujo de gases de escape de los ductos de salida, reduciendo las emisiones de material particulado a la atmósfera. El carbón utilizado puede ser bituminoso como subituminoso y se emplea en estado pulverizado.

La recepción del carbón se hace a través de Puerto Ventanas S.A., quien arrienda sus instalaciones a AES GENER para la recepción de carbón a través de barcos de graneles y su transporte hasta la cancha de almacenamiento es mediante cinta transportadora cubierta. Éste carbón es descargado en zonas de acopio mediante una correa giratoria y luego es distribuido mediante cargadores frontales para su posterior uso como combustible en las unidades de generación.

La empresa comercializa una parte del carbón recepcionado para clientes externos, además de despachar parte del combustible a la central Laguna Verde. Este combustible es cargado mediante correa transportadora a los camiones o bien directamente en la cancha de acopio mediante cargadores frontales.

La Central Termoeléctrica Nueva Ventanas es también de AES Gener y corresponde a la construcción y operación de una unidad generadora termoeléctrica tipo monoblock diseñada para consumir combustibles sólidos, carbón y/o coque de petróleo, por medio de una caldera de tecnología lecho fluidizado circulante.

5.- COMPAÑÍA DE PETRÓLEOS DE CHILE S.A. (COPEC).

Inicialmente se ubicaba en el sector de la Salinas en Viña del Mar y durante el año 2008 se instala en el borde de la Bahía de Quintero sector de Loncura.

La empresa COPEC es privada cuyo giro es la distribución de combustibles y lubricantes en todo el territorio nacional. En la Bahía de Quintero tiene un Terminal Marítimo y una Planta de Almacenamiento que forma parte de su Complejo Industrial Concón-Quintero.

6.- ENAP TERMINAL QUINTERO.

En el terminal Quintero de la Empresa Nacional de Petróleo, ENAP, se almacenan los petróleos crudos que son importados y transportados mediante embarcaciones marinas.

En la Bahía opera el Terminal Marítimo de Quintero, que se compone de un conjunto de instalaciones terrestres y marítimas destinadas a cargar y descargar buques, almacenando, y transfiriendo petróleo y derivados de petróleo entre la Refinería Aconcagua de Concón (de propiedad también de la empresa estatal) el terminal marítimo; alcanzando una superficie de alrededor de 405.000 m2.

7.- CENTRAL TERMOELÉCTRICA ENEL.

De propiedad de: Enel Generación Chile S.A. Se ubica en Ruta F30-E lote 2 Predio 16901, Quintero, Chile. Es una planta termoeléctrica ciclo simple de dos bloques con una potencia instalada de 257 MW.

8.- GASMAR S.A.

Empresa privada cuyo giro está centrado en la importación, transporte, almacenamiento, venta y distribución de gas licuado. En la comuna de Quintero, cuenta con un Terminal con cinco estanques de una capacidad de 145 mil m3.

El terminal presta regularmente servicios a los volúmenes de butano y propano con que ENAP abastece, por vía marítima, las demandas de sus clientes de la zona central de Chile. Bajo esta modalidad, ofrece servicios de descarga y carga de buques, almacenamiento de producto y su despacho hacia el oleoducto de SONACOL.

9.- OXIQUIM S.A.

Es una empresa privada que se especializa en la producción de “resinas para tableros de madera, servicios de terminales marítimos para graneles líquidos y en la comercialización y distribución de productos químicos y especialidades”. Cuenta con dos establecimientos en la zona de Ventanas, un Terminal Marítimo que descarga gráneles líquidos -metanol, estireno, acetato de etilo, etcétera- a través de ductos de descarga instalados en su muelle y un establecimiento de molienda de sustancias granulares, ubicado en el sector norte de la Bahía de Quintero, inmediatamente al sur del Puerto de Ventanas.

10.- PUERTO VENTANAS S.A.

Al comienzo de la década del noventa era un modesto muelle de tan solo 700 metros de longitud, tenía nada más que una grúa, con una cuchara para descarga de carbón, de aproximadamente 2 toneladas. Tenía dos patios de desembarque para naves de hasta 70.000 toneladas. Poseía también una correa transportadora de material, principalmente carbón para CHILECTRA. Los pilotes sostenían una vía transitable hasta su punta, mar adentro. Una empresa extranjera, cuyos principales accionistas, alemanes y españoles, se adjudicaron la totalidad de las instalaciones portuarias.

De acuerdo a la información de su sitio web, es uno de los puertos graneleros más importantes del país, con más de 27 años de historia. Esta empresa fue constituida en el año 1991 y fue adquiriendo progresivamente el puerto hasta el año 1994 en que se hizo de la propiedad total. Dentro de sus instalaciones se encuentran una bodega para Anglo American, empresa minera, con capacidad para 60.000 toneladas de concentrado de Cobre, un domo de almacenamiento de clinker para empresas Melón (cementos) y una cancha de acopio de carbón de petróleo para ENAP

La carga y la descarga de concentrado de cobre implican la manipulación de éste, no sólo a través de correas de transporte sino también por manejo de grúas, con exposición a la acción del viento. La posibilidad de caída al mar y contaminación consecuente de los sedimentos es evidente, lo que hace recomendable la instalación de sistema de protección para evitar polvo fugitivo.

11.- CORDEX ACTUAL PACSA.

Terminal de combustible y asfalto, PACSA, esta empresa se instala en el año 1999.

12.- TERMINAL DE GAS NATURAL LICUADO, GNL, EN QUINTERO.

Es el terminal de recepción, descarga, almacenamiento y regasificación de Gas Natural Licuado, GNL, que opera en la Bahía de Quintero y abastece de gas natural, a la zona central de Chile.

El terminal ocupa una superficie de 40 hectáreas en la Bahía de Quintero en el cual se construyeron los principales componentes de la planta: un muelle, tres estanques de almacenamiento que permiten la descarga de GNL y su almacenamiento en tierra, y una planta de regasificación. Cuenta con una capacidad total de 334 mil m3. Además, utiliza vaporizadores de panel abierto, que permite la producción de 15 millones de metros cúbicos de gas natural por día.

D) PLAN REGULADOR METROPOLITANO DE VALPARAÍSO, PREMVAL

Para una mejor comprensión de los hechos investigados, se encargó a la Biblioteca del Congreso Nacional [13] un estudio relacionado con la planificación territorial de la zona industrial de Quintero-Puchuncaví, del que se hizo una síntesis.

[13] Biblioteca del Congreso Nacional, Verónica de la Paz Mellado. Asesoría Técnica Parlamentaria.

La zona donde actualmente se emplaza la zona industrial de Ventanas, se encuentra ubicada entre los límites de las comunas de Quintero y Puchuncaví, fuera del área urbana de ambas comunas.

La regulación de este sector rural recae en la planificación intercomunal, en este caso el Plan Regulador Intercomunal. El instrumento que actualmente se encuentra vigente corresponde al Plan Intercomunal aprobado el 12 de enero de 1965.[14]

Desde hace más de 10 años, aproximadamente 1997, se encuentra en proceso de aprobación un nuevo instrumento de regulación intercomunal, sin embargo a la fecha este proceso no ha finalizado.

a) Plan Regulador Intercomunal de 1965[15].

El Plan Regulador Intercomunal de 1965[16] , contemplaba la creación de Zonas Satélites Industriales, que considerasen las posibilidades de desarrollo que ofrecían para la zona la fundición y refinería de cobre desde el año 1964.

Este Plan planteaba la necesidad de que estas zonas se constituyeran en polos laborales, con emplazamientos más próximos a las zonas habitacionales, y por otra parte, que en ellas se emplazaran las empresas peligrosas y molestas en zonas aisladas de las áreas urbanas, accesibles pero distantes.

Por otra parte, se contemplaban localizaciones especiales para aquellas empresas que requirieran del borde costero para su funcionamiento. Desde esta perspectiva, se aprobó -entre otras zonas en la provincia- la creación en la zona Puchuncaví- Quintero de dos áreas industriales[17]:

1) Zona E-9, correspondiente a una zona suburbana destinada a la instalación de industria peligrosa con una superficie de 226 hectáreas.

2) Zona E-10 correspondiente a una zona suburbana destinada a la instalación de industria molesta, con una superficie de 373 hectáreas.

Zonas industriales propuestas. Plan Intercomunal de 1965.

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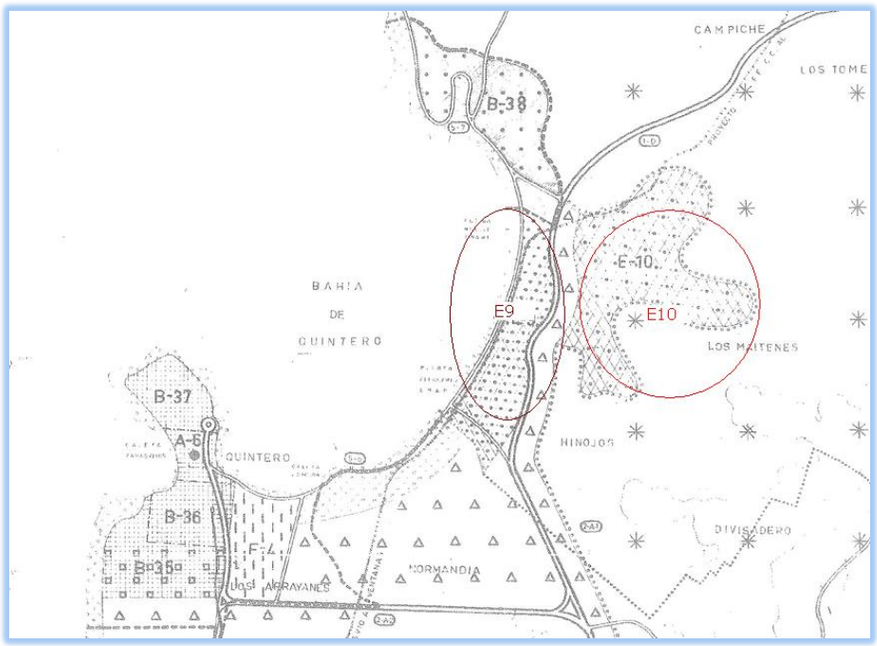
[14] Decreto N° 30, de 1965, Ministerio de Obras Públicas.
[15] Ibíd.
[16] Ordenanza del Plan Intercomunal de Valparaíso de 1965.(Junio 2011)
[17] Artículo 27 de Decreto N° 30, de 12 de enero de 1965, del Ministerio de Obras Públicas.



En el artículo 25[18] de este cuerpo normativo se establece la clasificación de las industrias, señalándose las siguientes categorías:

1.- Industrias peligrosas e insalubres:

Peligrosas: Son aquellas que por la índole eminentemente peligrosa de sus instalaciones, materias primas que en ella se emplean, productos intermedios o productos finales, pueden causar daños a las propiedades o salud pública, en un área que excede considerablemente los límites de su propio predio.

Insalubres: Aquellas en que las operaciones que se practican, procesos de fabricación, almacenamiento de materias primas o productos finales, que pueden producir emanaciones u olores que afectan a la salud pública.

2.- Industriales molestas:

Aquellas que pueden causar molestias a los residentes de las propiedades colindantes, producir excesivos ruidos o vibraciones, desprender humos o polvo, provocar excesivas concentraciones de tránsito o estacionamiento en las vías de uso público, causando con ello molestias que se prolonguen a cualquier período del día o de la noche.

3.- Industrias no molestas:

Aquellas que no producen daño ni molestias al resto de la comunidad, tales como micro zona industrial y artesanías al interior de las áreas urbanas.

Además, se establece un procedimiento para la clasificación de las industrias, el cual era de responsabilidad del Departamento de Higiene y Seguridad Industrial del Servicio de Salud, quien establecía su clasificación según las categorías

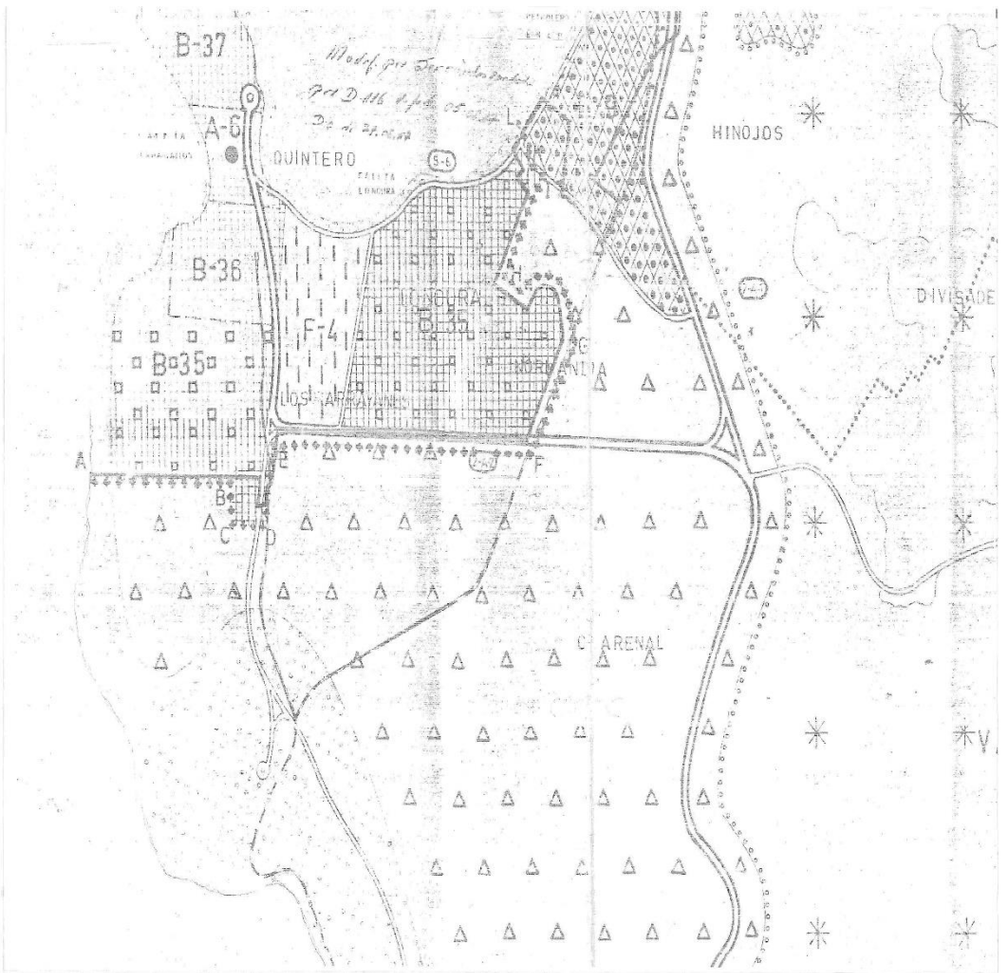
[18] Decreto N° 30, de 1965, del Ministerio de Obras Públicas. Versión original.

descritas. Con este pronunciamiento más el informe del asesor urbanista, en las comunas que corresponda, el Director de Obras se pronunciaba, sobre el tipo de zona que le correspondía a la industria en evaluación. Actualmente esta calificación es efectuada por la Secretaria Ministerial de Salud.

b) Primera modificación al Plan Regulador: Decreto N° 86, de 1984.[19]

En el año 1984 se aprobó la primera modificación con efectos sobre la zona Puchuncaví-Quintero. Los cambios apuntan a modificar el límite urbano de la ciudad de Quintero y los límites de la zona industrial E-9 destinada a industria peligrosa e insalubre.

Se aumenta el área de la zona de la industria peligrosa y se establece una zona de expansión urbana en Loncura, comuna de Quintero

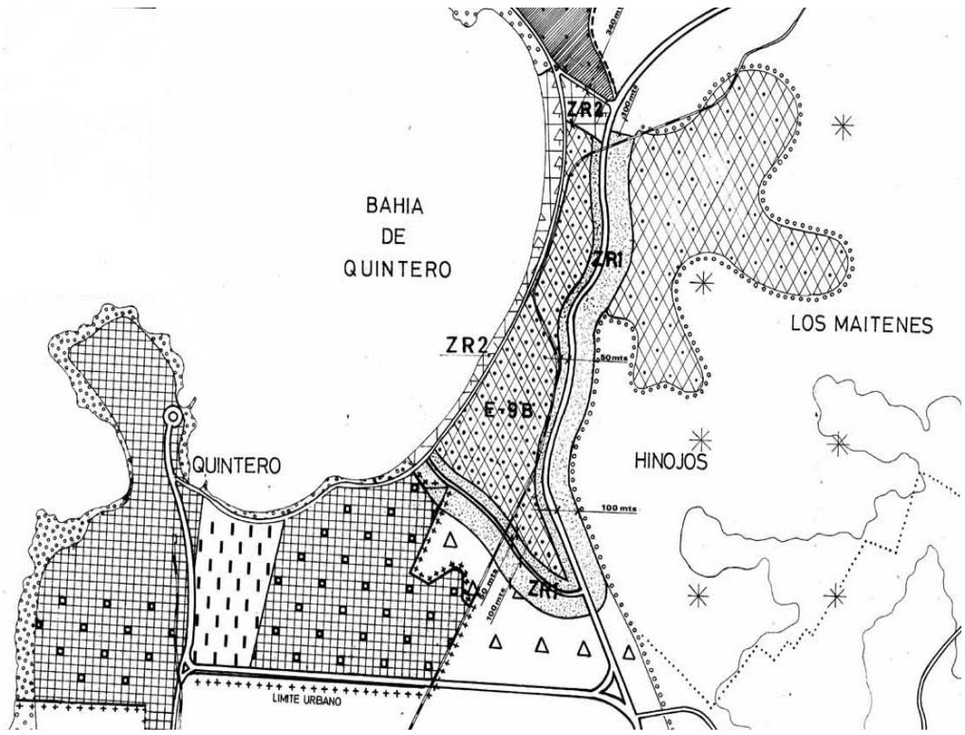


[19] Decreto N° 86, de 1984, Ministerio de Vivienda y Urbanismo.

c) Segunda modificación al Plan Regulador: Decreto N° 116, de 1987[20].

Este Decreto estableció nuevas zonificaciones y condiciones técnicas, en las zonas industriales peligrosas emplazadas en las comunas de Quintero y Puchuncaví. Entre ellas el establecimiento de zonas de restricción, y por otra a la especificación de las industrias calificadas como peligrosas.

Zonas industriales propuestas. Modificación Plan Intercomunal de 1987.



Las zonas de restricción constituidas se señalan en la siguiente tabla, y corresponde a franjas establecidas en el perímetro de la zona industrial peligrosa (E-9):

Zonas de restricción introducidas en la modificación.

Zona	Definición	Usos permitidos	Usos prohibidos
Zona ZR-1	Zona de restricción primaria de riesgo para el asentamiento humano.	Áreas verdes, cultivos agrícolas y forestación. Se podrán autorizar previo informe de la Secretaria Ministerial de Vivienda y Urbanismo de la región de Valparaíso, las instalaciones necesarias para su destino forestal y agrícola.	Subdivisiones inferiores a 5.000 m2. El emplazamiento de todo tipo de edificaciones destinadas a vivienda, equipamiento de cualquier escala o comercio, oficinas, camping transitorios o permanentes, balnearios de todo tipo, etc.

[20] Decreto N° 116, de 1987, Ministerio de Vivienda y Urbanismo.

Zona ZR-2	Zona de restricción primaria de riesgo para el asentamiento huma-no.	Solo se permitirá el desarrollo de áreas verdes y de áreas recreacionales vinculadas a las actividades propias del uso de las playas con sus instalaciones mínimas complementarias, calificadas como tales por la Secretaria Ministerial de Vivienda y Urbanismo, Región de Valparaíso, como ser sombreaderos, camarines transitorios, etc.	
Zona ZR-3	Zona de restricción primaria de riesgo para el asentamiento huma- no.	En esta zona no se permitirán subdivisiones, ni edificaciones, construcciones o instalaciones de ningún tipo.	

Decreto N° 116, de 1987, Ministerio de Vivienda y Urbanismo

Además, en esta modificación se incorporaron los siguientes conceptos relativos a las industrias peligrosas e insalubres:

a) Se incluyen en esta calificación las plantas de almacenamiento, distribución y procesamiento de combustibles, las plantas de producción y/o almacenamiento de gas y derivados del petróleo, las fábricas y/o almacenamiento de productos químicos, explosivos, polvóricos y/o inflamables, las fábricas y almacenamientos de explosivos, municiones y otros etc.

b) Para los efectos de la planificación estas instalaciones se consideraran siempre de carácter intercomunal, respecto del impacto que provocan en los sistemas funcionales urbanos y las áreas que los rodean.

c) Su emplazamiento sólo se permitía fuera de las áreas urbanas y contemplándose en cada caso las zonas de seguridad o restricción en torno a ellas, con las condiciones y características que permitan evitar el riesgo de la población y cautelar su funcionamiento.

d) Los estudios necesarios para cautelar las condiciones de seguridad debían ser realizados por la Secretaria Ministerial de Vivienda y Urbanismo, previa consulta a las instituciones competentes, aprobándose por decreto supremo.

d) Tercera modificación: Resolución N° 31-4-169 afecta de Gobierno Regional.[21]

En el año 1998 se realizó una nueva modificación. Se establecieron, nuevos usos de suelo, zonificación y vialidad, en el área denominada E-10 y en el área rural adyacente. Entre los cambios dispuestos se destacan:

a) Se reemplaza la zona E-10 por la denominación E-7A.

[21] Resolución N ° 31-4-169, afecta, Gobierno Regional de Valparaíso, de fecha 19 de enero de 1999.

Nombre de la zona industrial	**Comuna**	**Tipo de industria**	**Ubicación en área**	**Denominación en plano**
Ventanas	Puchuncaví Quintero	Peligrosa	Sub-urbana	E-7A

b) Para las industrias emplazadas en esta zona se establece la obligatoriedad de cumplir con las disposiciones sobre almacenamiento y transporte de gas licuado[22]; reglamento de seguridad para el almacenamiento, refinación, transporte y expendio al público de combustibles líquidos derivados del petróleo (derogado); ley N° 17.798 sobre control de armas, explosivos, y similares, y la ley N° 19.300.

c) Se agrega una zona de protección de cuenca y estero Campiche, destinado a proteger y preservar terrenos acuíferos y características de la cuenca vegetacional. En esta zona solo se permitirá el desarrollo de actividades que aseguren la permanencia de los valores naturales con las instalaciones y o edificaciones mínimas e indispensables para su habilitación, que se relacionen con la puesta en valor de los recursos naturales.

d) Se agrega una zona de restricción en torno a la vía 2 A 1 al oriente (marcada en azul) y a ambos lados de ruta 3-20.

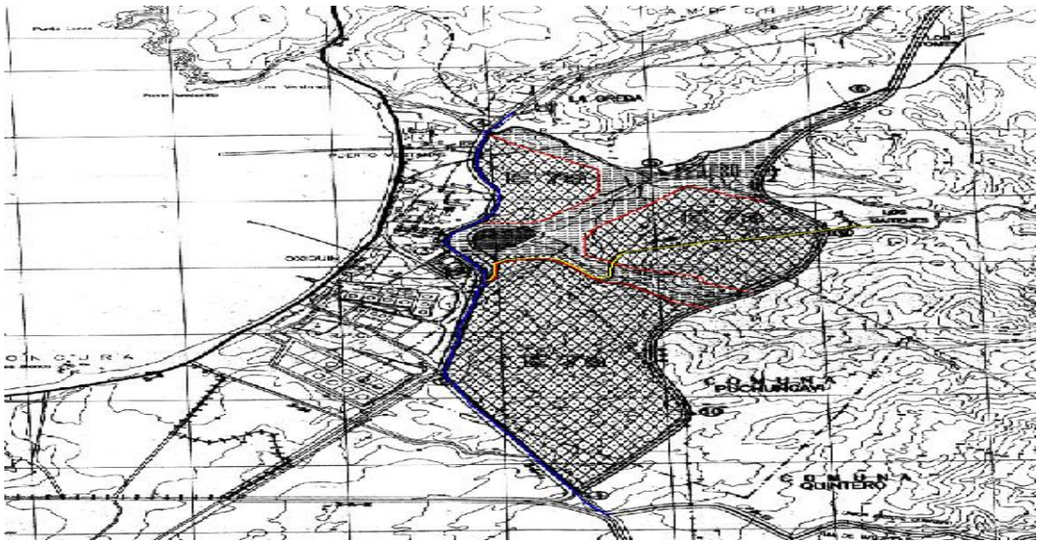
e) En la zona E7A, destinada a albergar industria catalogada como peligrosa y otros usos, se estableció que los usos permitidos corresponde a las instalaciones propias de las industrias peligrosas, provenientes de las necesidades de sus procesos específicos, construcciones de apoyo las que se fundamenten como necesidad al proceso industrial y al recurso humano que labora en la industria.

f) Los usos prohibidos son todos los indicados que no están expresamente incluidos entre los autorizados y se prohíbe expresamente la instalación de industrias que puedan afectar la calidad del aire con actividades que produzcan emanaciones u olores considerados incompatibles con los asentamientos poblacionales y la actividad turística de la zona, lo cual será evaluado en cada caso mediante el Estudio de Impacto Ambiental respectivo.

Se prohíbe la instalación de construcciones con destino habitacional permanente y transitorio, pudiendo instalarse solo aquellas necesaria para el cuidado de las instalaciones.

En síntesis se transforma zona de industria molesta en zona de industria peligrosa y se aumenta el área revista para este objeto.

[22] Decreto Supremo N° 29, de 1986, del Ministerio de Economía.



e) Cuarta modificación: Resolución N° 31-4-97 afecta de Gobierno Regional 2002.

En esta modificación, del año 2002, establece una nueva vialidad, usos de suelo y zonificación para la zona de restricción ZR-1, el sector suburbano adyacente ubicado entre el límite urbano comunal y las vías 2 A 1 y 2 A 2.

Las modificaciones introducidas establecieron los siguientes cambios: Se incorporan nuevos terrenos en las zonas de El Llano y Normandie, denominadas E 9 B1 y E 9 B2, con la siguiente zonificación:

Nombre de la zona industrial	Comuna	Tipo de industria	Ubicación en área	Denominación en plano
Ventanas	Puchuncaví Quintero	Peligrosa	Sub-urbana	E-9 B1
Ventanas	Quintero	No molesta	Sub-urbana	E-9 B2

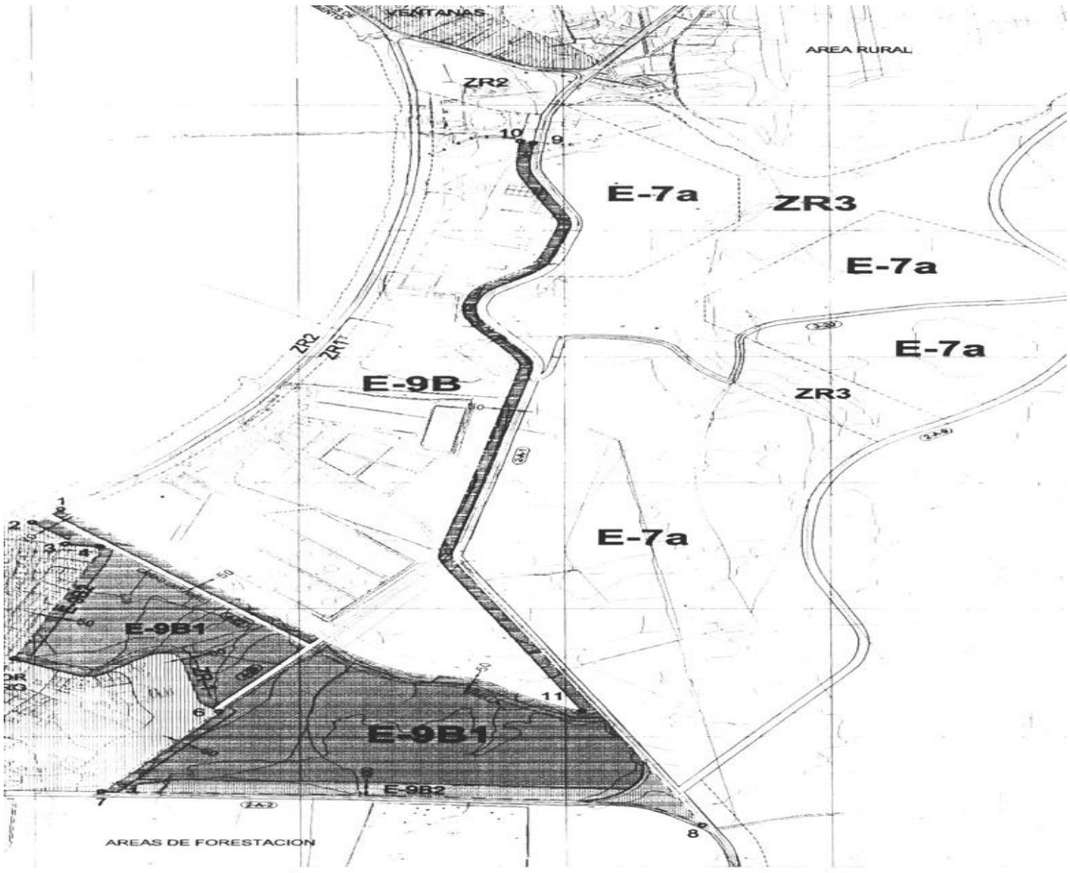
Los usos de suelo permitidos en estas áreas corresponderán a los siguientes:

- E-9.B.1: Industria peligrosa e insalubre, o industria molesta, con la excepción de cualquier tipo de explosivos y de instalaciones que involucren el uso de energía nuclear.

- E-9 B.2: Industrias no molestas y equipamiento de carácter complementario al uso industrial tales como oficinas y otros que sean parte del proyecto industrial o correspondan a ampliaciones del mismo proyecto. Además de equipamiento de tipo bancario, de alimentación y minimarket que ofrezca prestaciones directas al usuario de paso.

En ambas zonas el uso habitacional está prohibido excepto, aquella imprescindible para el personal que cumple funciones de vigilancia, emergencias y afines.

Modificaciones año 2002.



Se adjunta un plano en que se grafican las modificaciones desde el año 1984 a la del año 2002. En esta comparación es posible apreciar como se ha ido incrementando la zona que permite la instalación de industria peligrosa, tanto por la incorporación de nuevas áreas como por el cambio de los usos de otras.

Se aumenta la zona de industria peligrosa colindante con la zona de expansión urbana de Loncura, Quintero.

f) Plan Regulador Metropolitano de Valparaíso. Resolución 31/4 128 del Gobierno Regional de Valparaíso, de fecha 25 de Octubre de 2013. Plan Regulador Metropolitano de Valparaíso. Publicado el 2 de abril de 2014.

Mediante este instrumento se aprueba el Plan Regulador Metropolitano de Valparaíso, identificado como PREMVAL de Zonificación, Vialidad y Áreas Restringidas al Desarrollo Urbano; y se deroga el Plan Intercomunal de Valparaíso, aprobado por decreto 30 (MOP) de fecha 12 de enero de 1965, y sus modificaciones posteriores, con excepción de los actos administrativos que se detallan en dicho decreto, que particularmente en relación con el área estudio mantiene vigente la Resolución afecta Nº 31-4/97 (Gobierno Regional de la Región de Valparaíso) que aprueba la modificación al Plan Intercomunal de Valparaíso, sector El Llano y Normandie, comunas de Quintero y Puchuncaví, industrias peligrosas, molestas y no molestas, zonas E-9.B-1 y E-9.B-2. Este instrumento fue sometido al Sistema de Evaluación de Impacto Ambiental, mediante una Declaración de Impacto Ambiental

(DIA), la que fue calificada favorablemente mediante la Resolución Exenta N°21 de fecha 14 de febrero de 2011.

Respecto de la localización de las industrias calificadas como molestas, insalubres o contaminantes y peligrosas, el instrumento vigente señala:

"Por el impacto que provocan en los centros urbanos y en las áreas que los rodean, para efectos del presente Plan, el uso de suelo de actividades productivas que de conformidad a lo dispuesto en la Ordenanza General de Urbanismo y Construcciones sean calificadas como molestas, insalubres o contaminantes y peligrosas, ***se considerarán siempre de impacto intercomunal*** *y,* ***sólo podrán emplazarse en las zonas que expresamente se destinan para estos fines****.*

Las ***actividades productivas, que sean calificadas como peligrosas, no podrán emplazarse en áreas urbanas y sólo podrán hacerlo en las áreas de extensión urbana establecidas expresamente para ello****".*

Cabe hacer presente que esta denominación se rige por lo señalado en el artículo 4.14.2 de la Ordenanza General de Urbanismo y Construcción, según la consideración de la Secretaria Regional Ministerial de Salud; cuyas cuatro categorías son:

a. **Peligroso:** el que por el alto riesgo potencial permanente y por la índole eminentemente peligrosa, explosiva o nociva de sus procesos, materias primas, productos intermedios o finales o acopio de los mismos, pueden llegar a causar daño de carácter catastrófico para la salud o la propiedad, en un radio que excede los límites del propio predio.

b. **Insalubre o contaminante:** el que por destinación o por las operaciones o procesos que en ellos se practican o por los elementos que se acopian, dan lugar a consecuencias tales como vertimientos, desprendimientos, emanaciones, trepidaciones, ruidos, que puedan llegar a alterar el equilibrio del medio ambiente por el uso desmedido de la naturaleza o por la incorporación a la biósfera de sustancias extrañas, que perjudican directa o indirectamente la salud humana y ocasionen daños a los recursos agrícolas, forestales, pecuarios, piscícolas, u otros.

c. **Molesto:** aquel cuyo proceso de tratamientos de insumos, fabricación o almacenamiento de materias primas o productos finales, pueden ocasionalmente causar daños a la salud o la propiedad, y que normalmente quedan circunscritos al predio de la propia instalación, o bien, aquellos que puedan atraer insectos o roedores, producir ruidos o vibraciones, u otras consecuencias, causando con ello molestias que se prolonguen en cualquier período del día o de la noche.

d. **Inofensivo:** aquel que no produce daños ni molestias a la comunidad, personas o entorno, controlando y neutralizando los efectos del proceso productivo o de acopio, siempre dentro del propio predio e instalaciones, resultando éste inocuo.

La clasificación señalada, así como la zonificación prevista en la Ordenanza, no disponen de zonas de seguridad, ni se pronuncian respecto de la compatibilidad con las zonificaciones aledañas, aspecto que queda sujeto a lo previsto en el instrumento de planificación.

Respecto de otras consideraciones previstas en el instrumento de planificación intercomunal vigente, y que se relacionan con el emplazamiento de actividades en la zona en estudio se puede destacar que:

1. El artículo 4° señala una consideración respecto del emplazamiento de actividades productivas[23] y de infraestructura[24], de impacto intercomunal, en los casos en que el predio disponible se emplace en zonas con distintos usos de suelo. En tales casos, precisa que si al menos el 30% de la superficie permite el emplazamiento de las actividades señaladas, se permitirá su uso en todo el terreno. Esto se restringe para la comuna de Puchuncaví, no así en el caso de Quintero. Esta norma permitiría potencialmente el emplazamiento de actividades industriales en el perímetro de las zonas previstas.

2. El artículo 5° establece que en relación con los territorios que permiten la actividad industrial, aquellas instalaciones que sean calificadas de menor riesgo estarán siempre permitidas, sin perjuicio de que el instrumento de planificación comunal prohíba la aplicación de este artículo, excepto en la Comuna de Casablanca. Esto último no sucede en el sector en estudio.

3. En relación con las instalaciones destinada a infraestructura de impacto comunal el artículo 6° de instrumento citado precisa las siguientes:

- Infraestructura de transporte: Terminales de transporte terrestre asociados al transporte de carga, recintos marítimos o portuarios, instalaciones o recintos aeroportuarios.
- Infraestructura sanitaria: Plantas de captación, distribución o tratamiento de agua potable o de aguas servidas, rellenos sanitarios.
- Infraestructura energética: Centrales de generación o distribución de energía.

4. El artículo 33° reconoce las zonas destinadas a actividades productivas de alto impacto. Particularmente Quintero y Puchuncaví corresponde a la “Zona Productiva Peligrosa ZEU PP” y “Zona Productiva Peligrosa 1 ZEU PP 1”.

5. Asimismo, los artículos 36° y 37° del Plan Metropolitano de Valparaíso definen las condiciones exigibles a dichos predios.

6. En artículo 44° se define una zona de Infraestructura Aeroportuaria ZA, emplazada en la comuna de Quintero, en el sector de la Pista Aérea (Satélite Borde Costero Quintero-Puchuncaví). En dicho sector los usos de suelo permitido corresponden a infraestructura de transporte tales como instalaciones o recintos aeroportuarios, prohibiéndose todos los demás usos.

7. Entre las áreas protegidas por su valor natural y emplazadas aledañas al área en estudio se señala el Santuario de la naturaleza, Bosque de Las Petras, comuna de Quintero. DS Nº 278 del 7 junio 1993, protege 42 hectáreas. En dichas

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[23] Artículo 2.1.28 OGUC: “El tipo de uso Actividades Productivas comprende a todo tipo de industrias y aquellas instalaciones de impacto similar al industrial, tales como grandes depósitos, talleres o bodegas industriales. El Instrumento de Planificación Territorial podrá establecer limitaciones a su instalación, sin perjuicio del cumplimiento de las normas ambientales y demás disposiciones pertinentes”

[24] Artículo 2.1.29 OGUC: “El tipo de uso Infraestructura se refiere a las edificaciones o instalaciones y a las redes o trazados destinadas a: Infraestructura de transporte, tales como, vías y estaciones ferroviarias, terminales de transporte terrestre, recintos marítimos o portuarios, instalaciones o recintos aeroportuarios, etc.; Infraestructura sanitaria, tales como, plantas de captación, distribución o tratamiento de agua potable o de aguas servidas, de aguas lluvia, rellenos sanitarios, estaciones exclusivas de transferencia de residuos, etc.; e Infraestructura energética, tales como, centrales de generación o distribución de energía, de gas y de telecomunicaciones, gasoductos, etc. Las redes de distribución, redes de comunicaciones y de servicios domiciliarios y en general los trazados de infraestructura se entenderán siempre admitidos y se sujetarán a las disposiciones que establezcan los organismos competentes”.

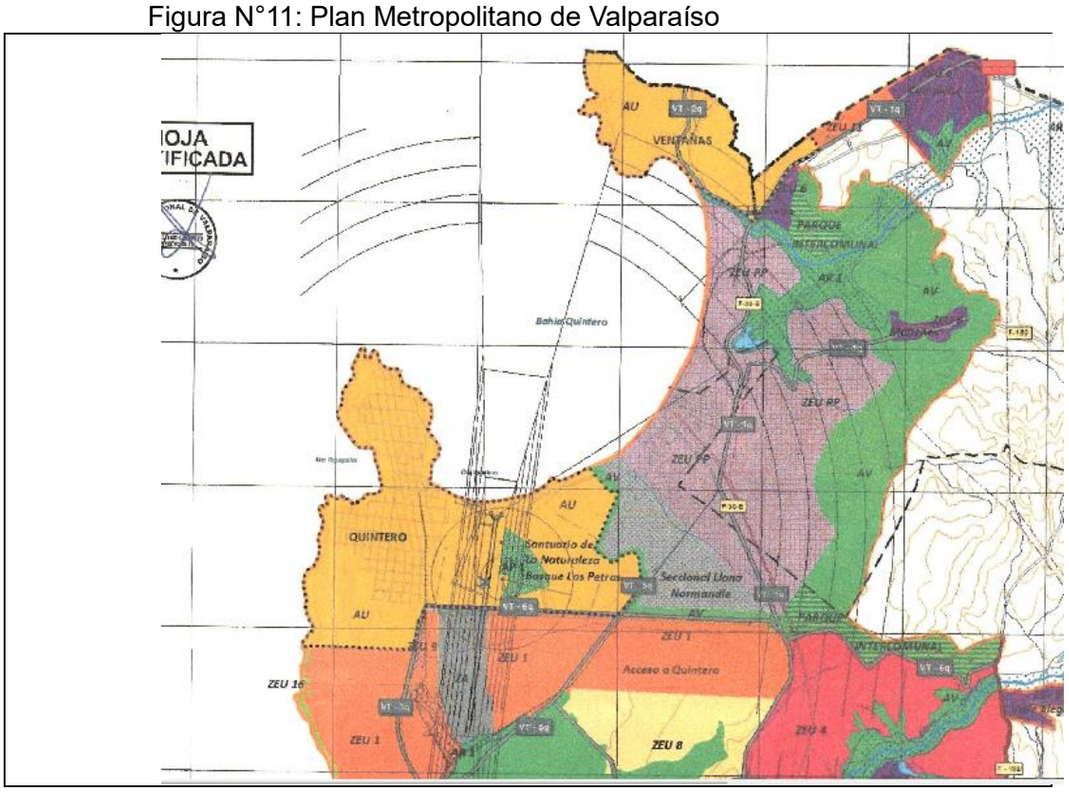
sectores solo se permiten los usos de suelo correspondientes a áreas verdes y edificaciones con destinos complementarios al área verde, referidas a construcciones complementarias a la recreación que no generan metros cuadrados construidos, tales como pérgolas, miradores, así como otro tipo de construcciones de carácter transitorio, tales como quioscos.

8. En el área en estudio se disponen dos parques intercomunales: Parque Intercomunal Quintero y Parque Intercomunal La Greda

9. Respecto de las áreas verdes en el Satélite Borde Costero Quintero – Puchuncaví se establecen las siguientes:

- AV Estero Puchuncaví: Área que comprende el estero del mismo nombre entre la Zona ZEU PP y AV Área Industrial, además de ZEU 6 Campiche.
- AV Área Industrial: Entre Maitenes y Valle Alegre.
- AV Sector Loncura: Faja en Sector Loncura y ruta F-210, entre ZEU 1 acceso a Quintero y Seccional Llano Normandie.

Figura N°11: Plan Metropolitano de Valparaíso



Fuente: Resolución 31/4 128 del Gobierno Regional de Valparaíso, de fecha 25 de Octubre de 2013

Evolución de las modificaciones al Plan Intercomunal de Valparaíso.

E) PROPUESTAS COMISIÓN INVESTIGADORA DEL AÑO 2011 Y ESTADO DE AVANCE.[25]

La comisión investigadora del año 2011 se formó por el incidente ambiental del 23 de marzo en Puchuncaví-Quintero. El resultado fue un documento que identificó responsabilidades en sectores del Estado y sus organismos de planificación y fiscalización, entendiendo como tales empresas estatales, ministerios sectoriales, servicios públicos relacionados con la fiscalización, gobierno regional y municipios, que conjuntamente a las empresas instaladas tienen responsabilidades directas e indirectas en la contaminación de la zona afectada. Adicionalmente, fueron formuladas recomendaciones que en este documento son contrastadas en acciones concretas para solucionar el problema crítico de contaminación de la zona.

La tabla de recomendaciones y acciones, incorporadas en este informe, muestra avances concretos que apuntan a la solución del problema, así como espacios para mejoras.

PPROPUESTAS	ACCIÓN
Es urgente y prioritario r**ealizar estudios que conduzcan a la remediación de los suelos aledaños a las zonas degradadas y a la Bahía de Quintero**. El Ministerio de Medio Ambiente, en coordinación con el Gobierno Regional de Valparaíso y el Ministerio de Salud debe asegurar los recursos necesarios para disponer de estos antecedentes y **elaborar así durante el año 2012 un Plan de Acción Integral para mejorar dicha situación**.	Informe final "Análisis de riesgo ecológico por sustancias potencialmente contaminantes en el aire, suelo y agua, en las comunas de Concón, Quintero y Puchuncaví". Noviembre 2013[26]. Informe final "Evaluación de exposición ambiental a sustancias potencialmente contaminantes presentes en el aire, comuna de Concón, Quintero y Puchuncaví". Septiembre 2013[27]. PRAS, Programa para la Recuperación Ambiental y Social Quintero Puchuncaví 2017[28].
Es necesario contar con **recursos asignados en la Ley de Presupuestos de la Nación** con la finalidad de realizar estudios y efectuar acciones de mitigación en las zonas impactadas por cada uno de estos episodios	El proyecto de presupuesto año 2019 no incluía los PRAS, sin embargo, a estos les fueron asignados 1.000 millones de pesos en su trámite legislativo. Además, la Glosa 05 indica: "La Subsecretaría del Medio Ambiente informará trimestralmente a la Comisión Especial Mixta de Presupuestos, a la Comisión de Medio Ambiente y Bienes Nacionales del Senado y a la de la Cámara de Diputados, sobre el estado de avance del Plan de Descontaminación Ventanas (Quintero y Puchuncaví), sus indicadores, evaluación y cronograma de trabajo"[29]
Es impostergable que la empresa CODELCO y todas las ubicadas en el parque industrial, presenten e inicien **en el año 2012 un plan de inversiones para controlar estas emisiones**…el resto de las empresas deben asumir acciones urgentes de mitigación, concordadas con las autoridades competentes.	En marzo del 2016 Codelco División Ventanas[30] declara que "se encuentra construyendo los más grandes proyectos ambientales de su historia, con una inversión que supera los US$160 millones, con el propósito de disminuir sus emisiones al ambiente y hacer más sustentable sus operaciones". Adicionalmente, los proyectos ya finalizados: "la edificación de un moderno centro de concentrado, la construcción de cerca de un kilómetro de cierres perimetrales, el aumento de captación de material particulado a través de en un tercer campo de Precipitador Electroestático y un nuevo filtro de mangas

[25] Biblioteca del Congreso Nacional. Abogado Enrique Vivanco Font, Asesoría Técnica Parlamentaria.
[26] Informe final "Análisis de riesgo ecológico por sustancias potencialmente contaminantes en el aire, suelo y agua, en las comunas de Concón, Quintero y Puchuncaví. Noviembre 2013. Centro de Ecología Aplicada. Disponible en: http://bcn.cl/28hpv (enero 2019).
[27] Informe final "Evaluación de exposición ambiental a sustancias potencialmente contaminantes presentes en el aire, comunas de Concón, Quintero y Puchuncaví". Septiembre 2013. Centro Nacional del Medio Ambiente (CENMA). Disponible en: http://bcn.cl/28hpw (enero 2019).
[28] PRAS, Programa para la Recuperación Ambiental y Social Quintero Puchuncaví 2017. Disponible en: http://bcn.cl/28hpx (enero 2019).
[29] Ley de presupuesto año 2019. Ministerio de Medio Ambiente. Subsecretaría de Medio Ambiente. Disponible en: http://bcn.cl/28hpy (enero 2019).
[30] CODELCO (marzo del 2016). Proyectos e inversiones Ventanas. Disponible en: http://bcn.cl/28hpz (enero 2019).

	del secador de concentrado, la alimentación de carga fría, entre otros". Las exigencias de captura y límites de emisión en chimeneas para el cumplimento del DS N° 28 entraron en vigencia para División Ventanas el 12 de diciembre de 2016. Se invirtieron US$ 105 millones y se logró cumplir con las emisiones y captaciones de azufre y arsénico, incluso por encima de lo exigido por la nueva normativa. En los reportes de sustentabilidad entre 2010 y 2017 CODELCO declara importantes inversiones en mejoras medio ambientales[31]. El Complejo Ventana firma el primero de diciembre de 2011 el Acuerdo de producción Limpia: Zona Industrial Puchuncaví-Quintero, Región de Valparaíso. El Complejo Ventana firma el primero de diciembre de 2011 el Acuerdo de producción Limpia: Zona Industrial Puchuncaví-Quintero, Región de Valparaíso.
Ante la falta de **estudios de línea base se evidencia la necesidad de elaborar un detallado estudio de líneas de bases de metales pesados** para iniciar así un programa de remediación de estos sectores.	Se dispone del Informe "Muestreo de los Suelos para las comunas de Quintero y Puchuncaví 2015"[32].
Las **estaciones de monitoreo de la zona industrial de Ventanas, se propone que éstas pasen a ser gestionadas por el Ministerio de Medio Ambiente** e incluidas dentro de la Red Nacional de Monitoreo de Calidad del Aire.	Desde el lunes 10 de septiembre de 2018 la red de monitoreo de calidad del aire pasa a ser supervisada de manera directa por el Estado de Chile. Del total de nueve estaciones, siete eran administradas por las empresas AES Gener y Codelco Ventanas, mientras que las otras dos eran propiedad de GNL Quintero y Enel. Actualmente, se dispone del "Portal red de monitoreo calidad del aire Complejo Industrial Ventanas"[33].
El **Plan de Descontaminación de Ventanas** aprobado por decreto supremo Nº 252 del año 1992, **se propone que sea reformulado**. El nuevo plan, abarque todo el complejo industrial Ventanas, con mesas de trabajo donde pueda participar la comunidad involucrada. Este nuevo plan de descontaminación deberá contar con actualizaciones de las normas medioambientales, incluyendo mediciones de SO2, MP10 y MP 2,5, así como establecer nuevos límites de emisión.	El Ministerio de Medio Ambiente ingresó el viernes 28 de diciembre de 2018 a la Contraloría General de la República el Plan de Prevención y Descontaminación Atmosférica (PPDA) para las comunas de Concón, Quintero y Puchuncaví. Sin información MP10 y MP 2,5.
Establecer el cofinanciamiento de un sistema de alarma preventiva, fondos de salud y recuperación de ecosistema, por las empresas que operan en la zona.	Sin información.
La Comisión estimó adecuado solicitar al Ejecutivo estudiar la viabilidad de implementar en el país un mecanismo **incorporando el monóxido de carbono así como otras alternativas de impuestos e incentivos verdes**.	Sin información respecto al uso de transacción de bonos de carbono en el Complejo Industrial de Ventanas. No obstante, en Chile desde el año 2011, se cuenta con la Bolsa del Clima de Santiago (SCX), que transa los bonos de carbono -Reducciones Certificadas de Emisiones de Gases Efecto Invernadero Además, el Ministerio de Medio Ambiente propuso "que en una primera fase las termoeléctricas puedan destinar entre un 15% a 20% del gravamen obligatorio a la compra de bonos de carbono de proyectos chilenos. Este planteamiento, ya se está discutiendo en el marco del *Program for Market Readiness* (PMR) que lidera Medio Ambiente junto al Ministerio de Energía"[34].

[31] CODELCO (s/f). Indicadores de sustentabilidad. Disponible en: http://bcn.cl/28hq0 (enero 2019).
[32] Informe final "Muestreo de los Suelos para las comunas de Quintero y Puchuncaví". PGS Chile. Disponible en: http://bcn.cl/28hq1 (enero 2019).
[33] Portal red de monitoreo calidad del aire Complejo Industrial Ventanas. Disponible en: http://bcn.cl/28hq2 (enero 2019).
[34] Electricidad (24 de mayo 2017). Cambio en impuesto verde impulsaría mercado de bonos de carbono. Disponible en: http://bcn.cl/28hq4 (enero 2018).

Es necesario **regular el efecto sinérgico y acumulativo de los proyectos que ingresen al SEIA** para lo cual la Comisión de Recursos Naturales, Bienes Nacionales y Medio Ambiente, con la asesoría de la Biblioteca del Congreso analizará la factibilidad de elaborar un proyecto de ley en tal sentido, incluyendo no sólo condicionantes medioambientales, sino que también parámetros máximos que permitan resguardar la salud de la población.	Sin información.
Instar al Ejecutivo que **modifique la regulación sobre la calificación industrial contenida en el artículo 4.14.2 de la Ordenanza General de Urbanismo y Construcción**, a fin de establecer parámetros objetivos que permitan la evaluación de todos los aspectos de una calificación industrial, comparable e incluyendo variables que caractericen adecuadamente tal actividad.	Texto del artículo 4.14.2 vigente desde año 2006. (Texto modificado por Decreto Supremo N° 193 de Ministerio de Vivienda y Urbanismo, de fecha 13 de enero de 2006). La única modificación del texto en el año 2006, respecto del texto original de la norma en su primera publicación, dice relación con el cambio de servicio responsable de la calificación, de Servicio de Salud del Ambiente a Secretaría Regional Ministerial de Salud[35].
El Ministerio de Medio Ambiente dicte a la brevedad una norma para fundiciones.	Decreto N° 28 establece norma de emisión para fundiciones de cobre y fuentes emisoras de arsénico. Publicación 12 de diciembre del 2013[36].
Sugerir al Ejecutivo, estudiar la viabilidad de elaborar un **plan de compensación** y ayuda destinado a resarcir, aunque sea parcialmente, los perjuicios sufridos por los trabajadores que acrediten, a través de informes médicos, que presentan algún trastorno, patología o cualquier otra afección derivada de la exposición a materias contaminantes en el periodo que realizaron trabajos para la Empresa Nacional de Minería y CODELCO.	El informe que fundamenta y entrega antecedentes para la elaboración del anteproyecto reformulación de Plan de descontaminación Ventanas, indica que "una fracción importante de los mecanismos de compensación comprometidos por los proyectos, no presentan criterios claros que den cuenta de la efectividad de las medidas, la trazabilidad ni la compatibilidad entre las fuentes involucradas en la compensación. Muchas veces, tampoco han permitido cuantificar la reducción de las emisiones como tampoco se ha tenido la certeza de las emisiones reales de cada fuente"[37]
Exámenes médicos obligatorios y periódicos a los trabajadores propios y contratistas de las distintas empresas que tienen actividades en la zona del complejo industrial. Proseguir con la **realización de exámenes a los habitantes de las zonas más contaminadas**, los que deben ser realizados en forma periódica y aleatoriamente.	A partir del evento de contaminación de marzo del 2011, el Instituto de Salud Pública (ISP) y Departamento de Salud Pública de la Pontificia Universidad Católica realizaron el análisis de los metales plomo en sangre; arsénico, cadmio, cromo y mercurio en orina. Se entregó el 29 de diciembre de 2011[38] Plan de salud comunal Puchuncaví 2013[39].
Instauración de **protocolos de avisos obligatorios, públicos y coordinados por parte de las empresas hacia los trabajadores, la comunidad y autoridades** correspondientes, en casos de episodios de emergencias, en tiempo real.	El Ministerio de Medio Ambiente planteó la necesidad de un protocolo para emergencias por contaminantes en Quintero y Puchuncaví. Hasta la fecha no se cuenta con el Plan de emergencia[40]
La Secretaría Regional Ministerial de Salud de Valparaíso, **debe identificar los lugares que presenten riesgo para la población en razón de la contaminación**, e instalar señalización clara y visible a fin de advertir de los riesgos que implica desarrollar alguna actividad en ellos.	El PRAS identifica riesgos que generan la contaminación para la población. Este programa fue construido sobre la base de los estudios realizados por Ministerio de Medio Ambiente y Ministerio de Salud y además de estudios privados.
Incorporar a las comunidades involucradas en el Plan Acuerdo de Producción Limpia (APL), suscrito entre el Ministerio de Medio Ambiente, Consejo Nacional de Producción Limpia y las empresas del	El APL del Complejo industrial Ventanas (Codelco Chile División Ventanas, Puerto Ventanas S.A., Aes Gener, Enap Refinerías, GNL Quintero, Gasmar, Melón, Oxiquim, Comercial Catamutun S.A.) es convenio de carácter

[35] DS N°47 DE Ministerio de Vivienda y Urbanismo. Disponible en: http://bcn.cl/28flv (enero 2019).
[36] Decreto N°28 establece norma de emisión para fundiciones de cobre y fuentes emisoras de arsénico. Publicación 12 de diciembre del 2013. Disponible en: http://bcn.cl/28hq5 (enero 2019).
[37] informe que fundamenta y entrega antecedentes para la elaboración del anteproyecto reformulación de plan de descontaminación Ventanas (2013). Disponible en: http://bcn.cl/28hq6 (enero 2019).
[38] ISP entrega resultados de estudios que determinan grado de exposición a metales de los residentes en la comuna de Puchuncaví, al Seremi del Medio Ambiente V Región. Disponible en: http://bcn.cl/28hq8 (enero 2019).
[39] Plan de salud comunal Puchuncaví 2013. Disponible en: http://bcn.cl/28hq9 (enero 2019)
[40] La larga espera por un protocolo para emergencias por contaminantes en Quintero y Puchuncaví (12 septiembre 2018). Disponible en: http://bcn.cl/28hqb (enero 2019).

complejo industrial, e informar a la población de su contenido.	voluntario celebrado entre una asociación empresarial representativa de un sector productivo y los organismos públicos (Ministerio de Medio Ambiente, Ministerio de Salud y autoridad marítima) competentes en materias ambientales, sanitarias, de higiene y seguridad laboral, eficiencia energética e hídrica y de fomento productivo, cuyo objetivo es aplicar la producción limpia. D.S. N° 346/94, Ministerio de Agricultura, "Declara zona saturada por anhídrido sulfuroso y material particulado al área circundante al complejo industrial ventanas, V Región. Vigente. También, se declara zona saturada por material particulado fino (MP2.5) en concentración anual, y de su condición de latente para la concentración diaria de MP2.5 y material particulado grueso (MP10), calificaciones que rigen desde 2015.
Solicitar al Presidente de la República que se estudie **la modificación del decreto supremo N° 113, de 2002, del Ministerio Secretaría General de la Presidencia, que establece normas primarias de calidad del aire para dióxido de azufre,** contemplando un nivel muy básico de emergencia ambiental en concentraciones de una hora y muy superior a los recomendados por organismos internacionales como la Organización Mundial de la Salud, que ha señalado que los efectos en el organismo de las personas para este contaminante, se producen con concentraciones muy inferiores a las que establece la norma vigente.	Norma horaria de SO2. El 28 de diciembre de 2018 ingreso de proyecto definitivo a Contraloría General.
Elaborar, a la brevedad, **normas primarias y secundarias de calidad de los suelos y de aguas.**	Sin información.
Establecer planes de descontaminación orientados no sólo a la calidad del aire, sino que también a la calidad de los suelos y aguas, en virtud de las distintas actividades que deben desplegarse para efectos de atenuar los daños ambientales que ya se han verificado, según consideraciones técnicas que armonicen la actividades de las industrias con la calidad de vida de las personas.	Sin información.
Todas las empresas del parque industrial deberían generar una inversión dirigida a la confección de un plan de recuperación y desarrollo sustentable de la biodiversidad y calidad de vida de las personas, y a partir de ello generar un trabajo conjunto con la comunidad, alcanzando de tal forma una convivencia armónica entre todos los actores.	Sin información.

III.-LABOR DESARROLLADA POR LA COMISIÓN.

Para dar cumplimiento a lo encomendado por la H. Corporación, la Comisión realizó un total de diecinueve sesiones y abordó su tarea sobre la base de un plan de trabajo propuesto por los Diputados miembros de ella. En virtud del mismo, durante su funcionamiento, citó y escuchó a los siguientes personeros, tanto del ámbito público como del privado, quienes la ilustraron sobre aspectos legales, técnicos y administrativos del problema:

1.- SEÑORA CAROLINA SCHMIDT, MINISTRA DE MEDIO AMBIENTE.

Señaló que la zona de Quintero y de Puchuncaví ha estado sometida por décadas a un proceso de contaminación continuo y permanente y ejemplificó diciendo que solo desde el 2008 a la fecha ha sufrido más de 300 varadas de carbón e innumerables derrames de petróleo.

En relación a la emergencia por contaminación explicó que las primeras medidas tomadas fueron declarar la alerta amarilla, establecer el hospital de campaña y fortalecer la red médica de salud.

Indicó que los días 21 y 23 de agosto se producen los dos primeros episodios de intoxicación. El 24 de agosto, la Superintendencia del Medio Ambiente, al encontrar evidencia de incumplimiento de normativa sanitaria que podría estar originando la contaminación, aplicó medidas precautorias para ordenar el cese inmediato de las faenas de limpieza en la planta de riles de una empresa de la zona. El 10 de septiembre, el gobierno toma la red de monitoreo de calidad del aire en manos de las empresas y la traspasa a la supervisión directa del Estado.

De manera adicional se compra un cromatógrafo, equipo altamente sofisticado que permite hacer análisis de calidad de gases, que se pondrá a disposición en la zona afectada el jueves 27 de septiembre.

A partir del primer semestre de 2019, se establecerá por primera vez en Chile una norma horaria para el control de la emisión de dióxido de azufre, pues la normativa vigente es laxa y además los niveles se exigen en promedios por día y año. Indicó que esta medida era importante por cuanto este gas es uno de los principales contaminantes de la zona.

Expresó que adicionalmente, el gobierno ingresó el viernes 21 de septiembre a la Contraloría General de la República, para toma de razón, el decreto que establece el estado de alerta sanitaria en la zona de Quintero-Puchuncaví, entregando facultades extraordinarias a la autoridad sanitaria para suspender faenas emisoras de gases contaminantes en todas las empresas de la zona. Añadió que paralelamente el Ministerio del Medio Ambiente alcanzó un histórico acuerdo con las compañías del cordón industrial para que suspendan inmediatamente, de manera voluntaria, las faenas contaminantes o riesgosas ante malas condiciones de ventilación presentes en la zona.

Al respecto precisó que cuando se analiza la situación de ventilación de la zona se observa que todos los episodios de concentración de gases ocurren cuando existe mala calidad del aire lo que ocurre durante las noches cuando existe mala ventilación, es decir en el período comprendido entre las 22.00 horas y las 8.00 de la mañana. En ese rango horario las empresas continúan su operación de manera regular y al bajar la temperatura, en particular cuando hay vaguada costera, se produce el aumento de la concentración de gases, con la consiguiente consciencia de que cuando las personas salen de sus casa respiran toda esa concentración.

Precisó que el decreto de alerta sanitaria obedece al interés del Estado de contar con la facultad de decretar de manera preventiva la paralización obligatoria de faenas ante situaciones de malas condiciones de ventilación y que estará vigente hasta que entren en marcha las soluciones de carácter más permanente y definitivo, que son las siguientes:

1) Endurecimiento de la normativa ambiental, que establecerá por primera vez en Chile una norma de control horaria del dióxido de azufre, el principal contaminante de esta zona, con el objeto de alcanzar los estándares de la Unión Europea.

2) Plan de Descontaminación Atmosférica para las comunas de Concón, Quintero y Puchuncaví que incorporará el control de emisiones de material particulado, dióxido de azufre y compuestos orgánicos volátiles, que son los famosos gases de hidrocarburos, que actualmente no se miden en la zona.

3) El control de la red de monitores por parte del Estado, lo que se concretó a partir del 10 de septiembre. Asimismo, indicó que el 27 de septiembre llegaría el cromatógrafo y así fortalecer las capacidades de medición, sin embargo, señaló que también era importante modernizar las demás capacidades de la red para medir de forma completa todos los gases que son relevantes de controlar en la zona, lo que se hará en base a la auditoría del gobierno de Finlandia.

4) Fortalecimiento de las capacidades de monitoreo local, dotando a los municipios de Concón, Quintero y Puchuncaví de monitores de tipo screening, que llegarán a partir de noviembre de este año.

Explicó que esta alerta sanitaria la implementaría el Ministerio de Salud con la colaboración del Ministerio del Medio Ambiente en los siguientes tres ejes:

a) El seguimiento diario de la calidad del aire y pronóstico de la ventilación de la zona, a cargo del Ministerio del Medio Ambiente.

b) La exigencia de planes operacionales a las empresas de la zona para reducir emisiones y suspender faenas contaminantes en períodos con pronóstico de mala ventilación, medida que deberá ser implementada por la Seremi de Salud, quien solicitará con carácter de urgente los planes operacionales a las industrias una vez que entre en vigencia el decreto de alerta sanitaria y, de este modo, podrá suspender obligatoriamente las faenas contaminantes.

c) El fortalecimiento de la fiscalización. El decreto de alerta sanitaria permite a la Seremi de Salud reorientar y focalizar recursos para fiscalizar el cumplimiento de los planes operacionales.

Aseveró que con todas estas medidas se lograría concatenar el decreto de alerta sanitaria y con la entrada en vigencia de las medidas permanentes que contribuirán en parte a la solución de la contaminación de la zona y que son: el plan de descontaminación para la zona de Quintero y Puchuncaví y la norma horaria de dióxido de azufre.

Acera de las medidas de calidad del aire, precisó que existían dos tipos de medición, una, de concentración de calidad del aire y, otra, de emisión de gases contaminantes por las empresas. Por lo tanto, la ventilación no es el único factor que influye en la contaminación. Las normas de concentración y de emisión deben ser revisadas conjuntamente, de ahí la importancia de robustecer y endurecer la normativa de emisiones.

Explicó que en la normativa sobre concentración de gases jugaba un papel importante la condiciones de ventilación ya que si esta es mala existirán mayores posibilidades de concentración de materia particulado y de gases y, con ello, peligro de intoxicación para la población.

En relación con los responsables de la situación contestó que era algo que debía contestar la Superintendencia del Medio Ambiente como organismo autónomo, facultado para investigar, fiscalizar y sancionar.

Respecto al papel del Ministerio del Medio Ambiente en la alerta sanitaria, puntualizó que las facultades, por normativa –Código de Salud-, recaen en el Ministerio de Salud, pero se disponen recursos especiales para fiscalización.

En cuanto al establecimiento de normas primarias de suelo, respondió que el gobierno estaba concentrado en las primeras medidas del plan integral de descontaminación para la zona de Quintero y Puchuncaví, específicamente a la contaminación del aire, no obstante, aseveró que se tiene contemplado avanzar en temas de suelo y de agua.

Sobre la tipificación de los delitos medioambientales, indicó que para este gobierno establecer sanciones penales para delitos medioambientales era una prioridad. De hecho, agregó que, el proyecto de modernización del Código Penal presentado por el Gobierno del Presidente Sebastián Piñera en marzo de 2014, los contempla.

Sobre la norma horaria, explicó que se optó por ella y no por la minutual porque cuando se enciende se produce una descarga más grande de material. Afirmó que así lo había establecido la norma internacional y de ahí que las empresas tendrán la obligación de adecuar su tecnología.

Sostuvo que para que las normas sean efectivas y no letra muerta era importante que contemplar un plazo de adaptación y así se permitan realizar las inversiones necesarias.

2.- SEÑOR EMILIO SANTELICES, MINISTRO DE SALUD.

Indicó que esta zona tiene un pasivo ambiental muy importante. La red de monitoreo, instalada desde 1992 y que cuenta con ocho estaciones, está a cargo de las mismas empresas, con una alta concentración de emisiones de contaminantes en toda la región. Tiene un plan de descontaminación del Ministerio de Minería, vigente del año 1992, enfocado a disminuir emisiones en solo dos empresas.

Señaló que existen 19 empresas operando en la Bahía. 14 de ellas (73,6%) en la Comuna de Puchuncaví y 5 en la Comuna de Quintero (26,4%) y que las principales actividades desarrolladas en el complejo industrial ventana son

a) Producción energética, entre ellas: • fundición de cobre, •centrales termoeléctricas a carbón y a gas, • almacenamiento de gas natural, carbón, petcoke, concentrado de cu, escorias, clinker, cenizas y combustibles líquidos, • embarque y desembarque de materias primas (sustancias químicas peligrosas, por ejemplo);

b) cementera;

c) industrias químicas, y

d) transporte y almacenamiento de sustancias peligrosas.

Afirmó que de acuerdo a las condiciones geográficas de la bahía de Quintero y Puchuncaví, existe una complejidad en la meteorología y que cuando convergen las condiciones medioambientales con el aumento de los peaks, se genera una sinergia. Entonces es posible utilizar la predicción de las condiciones medioambientales sin la necesidad de contar con una metodología específica.

Expresó que la alerta sanitaria entregó las prerrogativas jurídicas para hacer intervenciones y tempranamente generar la prohibición de funcionamiento de todas aquellas empresas que no cumplieron con los estándares. Como consecuencia, se obligó a las industrias de la zona a disminuir las emisiones de dióxido de azufre en un 20%, porcentaje que podrá aumentar si las condiciones así lo ameritan y se restringió totalmente la emisión de compuestos orgánicos volátiles, asociados a la mala ventilación. A su vez, a las empresas se les exigió entregar sus planes operacionales y los servicios públicos, organismos de la administración del Estado y otras entidades públicas o privadas, deberán colaborar para el cumplimiento de estas medidas. Informó que a partir de la normativa y de las prerrogativas indicadas se inició el control inmediato de la zona desde el punto de vista de la salud.

Indico que las prerrogativas de la alerta sanitaria también permiten deterger la marcha de las empresas si las condiciones lo ameritan y es así como ha habido interrupción de algunas faenas específicas, a la luz de las condiciones ambientales.

En términos del proceso de atención de los pacientes, entre otras medidas, se realizó un reforzamiento de la atención sanitaria: se instaló un puesto médico de avanzada, con especialistas en broncopulmonar, neurología, toxicología y pediatría. En una segunda etapa, se instalaron médicos urgenciólogos, asociados a los médicos que ya existían en el hospital, para hacer un mejor tamizaje de las poblaciones y descargar a los médicos que estaban en su régimen, para atender a los enfermos que venían por otro tipo de consulta. Además se estableció un apoyo a la atención de salud, a través de telemedicina, en distintas vertientes: telecardiología, teleradiología e incluso interconsulta. También se reforzó el equipamiento del hospital incorporando electrocardiogramas, equipos de oxigenoterapia y otros equipos de monitoreo, fundamentalmente oximetría.

Explicó que el papel del toxicólogo fue entregar orientación a los equipos de salud, y posteriormente, quedó de manera intercurrente, asistiendo algunas horas al día. Paralelamente se suscribió un acuerdo con el Cituc (Centro de Información Toxicológica de la Pontificia Universidad Católica de Chile) que se desarrolla en dos ámbitos de acción, uno consistió en estudios y análisis de la problemática global para la generación de propuestas y soluciones en el largo plazo y el segundo ámbito se refiere a la interpretación de los datos recopilados, respecto de los instrumentos utilizando y las medicioneobtenidas.

Señaló que la contribución del Citu fue en cuanto a la forma en que se manejó el tema de los toxicólogos, indicando que ayudó en el tema inmediato realizando atención clínica e interpretaron los primeros datos, además de colaborar en la estructuración orientada al trabajo de más largo plazo.

Informó que el examen para advertir intoxicación por monóxido de carbono es la medición de la carboxihemoglobina, y éste se implementó de manera inmediata, agregó que respecto a los otros gases no existe un instrumento para medirlos, descartando la realización de exámenes de sangre como instrumento adecuado. En consecuencia la aproximación más importante tiene que ver con el correlato de la sintomatología clínica y con lo indicado por los instrumentos medioambientales. Indicó que se incorporó un equipo para medir carboxihemoglobina en la etapa inicial.

Explicó que para medir los metales pesados existentes en agua y tierra, se requiere de una metodología, además de hacer una calicata que debe superar los diez centímetros hacia abajo, además debe haber una georreferenciación, de modo que exista una muestra representativa del lugar. Mientras que en los términos de salud puede medirse a través de exámenes de orina.

Manifestó que hubo alta con seguimientos programados fue respecto de 958 pacientes, y que se indicó la realización de evaluación neurológica respecto de 58 pacientes, y 8 con reevaluación pediátrica. Agregó que el alta sin seguimiento programado, fue de 30%. Agregando que de los totales citados, los pacientes que no se presentaron alcanzaron el 35%; mientras que los pacientes con seguimiento inicial completo corresponden al 57%; en el caso de evaluación broncopulmonar 140, y evaluación neurológica 58. Además, sostuvo que las personas dadas de alta corresponden a 120, mientras que las personas que continúan en seguimiento por exámenes complementarios alcanzan a 478.

Sostuvo que en relación con el horario de los hospitales de campaña, inicialmente se tuvo como expectativa trabajar durante 24 horas. Sin embargo, evidenció que al cabo de dos o tres días, con mayor tranquilidad y debido a la demanda, quedaron funcionando solo de día, toda vez que en las noches no se requería su funcionamiento. Indico que producto de lo anterior, muchas personas pensaron que el hospital no contaba con la capacidad necesaria para atender a los pacientes, pese a que en realidad la capacidad del hospital estuvo siempre adecuadamente resueltas. Indicó que ello formó parte del informe evacuado por la Organización Mundial de la Salud y la Organización Panamericana de la Salud.

Indico, que durante este período se realizó una inversión de alrededor de 120 millones de pesos y afirmó que en atención de salud la situación estaba resuelta a corto plazo y también en el largo plazo, en términos estructurales, concibiendo la infraestructura, el equipamiento y el personal.

Precisó que el hospital de Quintero tiene una serie de deficiencias estructurales: techumbre, red eléctrica y red de oxígeno y que antes de las emergencias ambientales se estaba desarrollando un plan para subsanarlas. Paralelamente se están definiendo estudios para un nuevo hospital en la red, en la zona, y también se está definiendo, como otra medida más estructural, la construcción de un Cesfam para Quintero. Agregó que el segundo Cesfam de Puchuncaví está en construcción, con un 12 por ciento de avance. Se trató de acelerar su construcción, pero las negociaciones con la constructora fueron infructuosas por ello el Servicio de Salud Viña del Mar Quillota va a relicitar el segundo Cesfam de Puchuncaví.

Como medidas sanitarias de largo plazo, está en proceso de diseño para licitación un nuevo laboratorio medioambiental, que se va a construir en Quilpué, y que estará dotado de todas las características y condiciones para soportar las necesidades medioambientales de esta zona.

Sostuvo que desde el Ministerio se ha reforzado, desde el área de la salud pública, el Departamento de Epidemiología Medioambiental, para levantar los mapas de riesgo a fin de contar con una estrategia anticipatoria en materias medioambientales a lo largo de todo el país, identificando aquellos potenciales focos de amenaza a las condiciones de salud de la población.

3.- SEÑORA MARÍA VICTORIA GAZMURI, SEREMI DEL MEDIO AMBIENTE DE LA REGIÓN DE VALPARAÍSO.

Precisó que desde el momento en que asumió el gobierno, han estado trabajando por la situación de Quintero y Puchuncaví, aclarando que las labores no comenzaron a partir del 21 o del 23 de agosto. Así el 20 de agosto, a menos de 24 horas antes de lo episodios de contaminación hubo una reunión entre la Ministra Carolina Schmidt, los alcaldes de las comunas y los diputados Luis Pardo y Camila Flores, en que el gobierno se comprometió a acelerar las gestiones del plan de descontaminación, a avanzar en la línea de una red de monitoreo con el objeto de otorgar confianza y legitimidad a las mediciones realizadas, además, de efectuar gestiones con la Superintendencia del Medio Ambiente en materia de fiscalizaciones preventivas y permanentes.

Por otra parte precisó que estos episodios de intoxicación por aire no han sido únicos ya que la zona lleva más de 50 años expuesta a otros contaminantes como derrame de petróleo, varamiento de residuos de carbón y episodios agudos de contaminación atmosférica. Así el 22 de julio se produjo un derrame en el estero Santa Julia, al que acudió de inmediato junto con los encargados municipales, sin embargo, producto de la lentitud y falta de respuesta de la empresa que se encontraba efectuando labores, se decidió judicializar la situación y la Ministra de Educación remitió los antecedentes ante el Consejo de Defensa del Estado.

Producida la emergencia, indicó que la Ministra del Medio Ambiente tomó contacto de inmediato, dando la instrucción de tomar las medidas correspondientes. Agregó que el trabajo desarrollado por los vecinos, diputados y autoridades, ha sido colaborativo, tomando el control de las actividades el intendente y la Ministra, siendo lo fundamental escuchar y buscar soluciones, considerando el trabajo efectuado con anterioridad por el Consejo para la Recuperación Ambiental y Social, que se encuentra plasmado en el PRAS (Programa para la Recuperación Ambiental y Social), así muchas de las medidas desarrolladas se han trabajado en conjunto.

Indicó que en Chile no existen normativas que regulen los hidrocarburos y los diferentes compuestos; las emisiones de hidrocarburos son parte de los compuestos orgánicos volátiles. Dentro de estos compuestos orgánicos volátiles, que va a abordar el nuevo proyecto del plan de descontaminación, en forma inédita, se dividen en artificiales y naturales. Dentro de los artificiales están los derivados de hidrocarburos. Estos básicamente son cadenas, pueden ser cíclicos, aromáticos, lo BTX están incluidos ahí, etcétera. Estas cadenas de hidrocarburos se combinan con otros compuestos en el aire y pueden –perdonen la vulgaridad- perder eslabones en estas cadenas y generar sintomatologías diferentes. Agregó que estos compuestos permanecen por varios días, incluso, semanas o meses en la atmósfera, por lo tanto, ello dificulta establecer la causalidad, y puede ser que lo que haya salido en fuente x sea x1 y que, finalmente, se mezcló en la atmósfera con otros compuestos y terminó transformándose en x2 o x3, incluso, x4. En ese sentido, el Ministerio de Salud tiene un convenio con el Centro de Toxicología de la Universidad Católica, y el doctor Juan Carlos Ríos es quien está dirigiendo el tema de emisiones que se están realizando con un equipo de cromatógrafos espectógrafos de masas, que es el equipo nuevo que se está usando, pues no existía ninguno en el país; en Latinoamérica creo que había uno.

Acerca de las mediciones de calidad del aire, consideró fundamental, necesario y prioritario dar seguridad y certeza a la comunidad en orden a determinar

qué aire se está respirando. Por ello, señaló el compromiso adquirido por el gobierno en relación a llevar las mediciones a estándares internacionales, de manera independiente y externa.

Para ello buscó modernizar las redes de monitoreo de calidad del aire, incorporando un cromatógrafo que permitirá fortalecer las capacidades de medición. Modernización de la red actual en base a los resultados de la auditoria que realizará el gobierno de Finlandia. Se logró un acuerdo porque Finlandia posee altos estándares en materia medioambiental respecto a realizar diagnósticos en la red actual de monitoreo. Agregó que dicha medida constituye un piloto que va a realizarse en las zonas de Concón, Quintero y Puchuncaví, el que probablemente va a servir para el resto de las comunas y las regiones de Chile. Destacó que dicho plan piloto es inédito, el que significará pasar a la vanguardia de toda América Latina en relación con la medición y monitoreo de la calidad del aire y, además, significará una modernización y actualización de los estándares existentes en Chile, siguiendo los pasos de países europeos.

Señaló que de esta manera, se indicará aquello que se debe medir, dónde se debe medir, y como pedir. Agregó que tales medidas serán implementadas a partir del segundo semestre del próximo año. Indicó que dentro del compromiso firmado con el gobierno de Finlandia, se realizarán auditorías una vez al año, con estándares de la Comunidad Europea, con la finalidad de verificar la calidad de aire que se está respirando.

Insistió en la dificultad de conocer cuáles son los contaminantes en una red de monitoreo que une seis compuestos, entre cuatro y seis compuestos, sin embargo se ha avanzado en mediciones que nunca antes se habían hecho a través del equipo que otorgó el Ministerio de Medio Ambiente, el equipo especial Miran, de tecnología infrarroja, y el equipo del cromatógrafo a través de la cromatografía y la separación de los gases.

Consultada acerca de la fiabilidad de los resultados que arrojó el primer equipo detector utilizado, el Miran XL, que acusó la presencia de nitrobenceno, isobutano y metilcloroformo, indicó que este equipo utiliza una tecnología infrarroja, es decir está preparado para medir en altas concentraciones, pues cuando hay bajas concentraciones, baja su índice de confiabilidad y agregó que ninguno de los químicos detectados superó el nivel de sensibilidad mínimo (80%) que el Miran XL requiere para arrojar un resultado fiable.

Agregó que el cromatógrafo es más sensible y puede detectar compuestos específicos con una confiabilidad incluso mayor a 90 o 95 por ciento en algunos casos, por lo que es un instrumento mucho más especializado en el proceso de detectar compuestos específicos en bajas concentraciones.

Explicó que se encuentran elaborando un nuevo plan de descontaminación y para ello se están recabando antecedentes e indicó que se han recibido más de 25 ingresos durante los primeros diez días desde el momento en que se publicó la resolución. Además, señaló que se encuentran consolidando la información y preparando el anteproyecto, que va a ser publicado el 31 de octubre, para que entre el 5 de noviembre y el 14 de diciembre se realice el proceso de participación ciudadana, con una buena difusión previa, toda vez que en el plan de descontaminación anterior se realizaron tres talleres de participación, con un total de 169 participantes entre las tres comunas, lo que evidencia una participación bastante baja, mientras que, en el nuevo período, el gobierno se ha comprometido a realizar al

menor 8 instancias de participación ciudadana presencial, más instancias de tipo digital.

En efecto, en el nuevo proceso de participación, con la solicitud de algunos de los consejeros del CRAS, se acordó realizar talleres, además de conformar un diálogo participativo abierto, con la finalidad de realizar una conversación fructífera y con mayor riqueza, donde las personas espontáneamente acudan y se encuentren con especialistas y profesionales que responderán sus consultas incluso preguntas que hayan surgido en diálogos participativos anteriores, con el objeto de recoger el pensamiento, sentir, inquietudes y anhelos de la comunidad y traducirlo en sugerencias que se implementar en los planes de descontaminación. Agregó que el diálogo participativo es una modalidad en la que primero se realiza una exposición, donde posteriormente, se reúnen en grupos pequeños, en donde se entrega una minuta explicativa donde se incluyen gráficos para traducirla a un lenguaje más entendible para todos. Además se entregará una minuta orientadora para hacer un poco más amigable y gráfico los contenidos y las ideas fuerzas del plan. Posteriormente se formarán grupos, donde existirán moderadores con *know-how* en temas de participación ciudadana; ello, con la finalidad de generar conversaciones a través de un cuestionario orientador, que permita encausar este diálogo. Explicó que la idea de ello es que cada uno los grupos lleguen a conclusiones generales, las que serán expuestas en un formato tipo plenario, de manera que queden plasmadas.

Aseguró que toda la información estará disponible en la plataforma web, con el objeto de que cualquiera de los vecinos pueda efectuar consultas o sugerencias. Aclaró que lo que se busca con lo anteriormente planteado es generar una instancia de “casa abierta”, donde exista disponibilidad para que los vecinos, de acuerdo a sus horarios, puedan hacer las consultas que estimen convenientes y aclaren sus dudas.

Sin embargo reconoció la necesidad de contar con ayuda para solucionar la situación de las zonas afectadas, destacando las labores desarrolladas por el Consejo para la Recuperación Ambiental y Social que tiene medidas bastante potentes y por ello se está haciendo un seguimiento para abordar cada una de esas medidas, sobre todo las que tienen que ver con la contaminación de la zona.

Consultada sobre la razón por la que no se paralizó el cordón industrial, señalo que la alerta sanitaria decretada por el Ministerio de Salud a través de la dictación del decreto 83, de 24 de septiembre, otorgó la facultad a la Seremi de Salud de solicitar la reducción de las emisiones cuando las condiciones de ventilación en la bahía de Quintero-Puchuncaví no fueran las adecuadas. Adicionalmente, ese decreto establece la condición de ingresar al 31 de diciembre la nueva norma de regulación ambiental para Concón, Quintero y Puchuncaví y también ingresar al 31 de diciembre de 2018 la norma horaria de emisión de dióxido de azufre

Respecto de lo que establece el decreto de alerta sanitaria, las empresas han entregado planes operacionales que han sido observados y revisados por un equipo multidisciplinario intersectorial que incluyó al Ministerio de Salud, a la Superintendencia del Medio Ambiente, Seremi de Medio Ambiente, el Ministerio del Medio Ambiente y a los servicios relacionados y cada una de las empresas se comprometen a adoptar diferentes medidas operacionales o de gestión para reducir sus emisiones en caso de que las condiciones de ventilación no sean las adecuadas. Explicó que por ello la mayor parte de las noches, entre las 12 y las 7 de la mañana,

las condiciones meteorológicas y se analizan de acuerdo a la información que entrega diariamente la Dirección Meteorológica de Chile, si las condiciones de ventilación son adversas, las empresas bajan su nivel de operación e implementan sus planes operacionales para actuar bajo las condiciones de alerta sanitaria.

Explicó que el Ministerio del Medio Ambiente tiene facultades en prevención, en normas, en planes y programas que competen al tema ambiental, pero la fiscalización y medidas sancionatorias competen al Ministerio de Salud y a la Superintendencia del Medio Ambiente. Agregó que esta última formuló cargos sancionatorios a cuatro empresas del sector, y el Ministerio de Salud ha levantado más de 17 sumarios sanitarios a diferentes empresas.

Indicó que se está haciendo un esfuerzo de fiscalización 24/7, día y noche fiscalizando las empresas, porque al Ministerio le interesa seguir avanzando en el desarrollo de la normativa y del plan de descontaminación y la norma horaria para las emisiones.

Finalmente, manifestó la necesidad de aumentar la cantidad de recursos para la Superintendencia del Medio Ambiente, que permitan fortalecer la fiscalización, además de continuar avanzando en materia de legislación ambiental, cumpliendo con los estándares internacionales establecidos.

4.- SEÑOR FRANCISCO ÁLVAREZ ROMÁN, SEREMI DE SALUD DE LA REGIÓN DE VALPARAÍSO.

Lamentó la cantidad de personas que tuvieron esta sintomatología, cifra que llegó a las 1.370 personas, sin embargo, sostuvo que a partir del 4 de octubre, en que se anunció el Decreto Supremo 83 del Ministerio de Salud que declaró Alerta Sanitaria, el número de atenciones en los centros de salud experimentó una disminución en del 85%, respecto al peak de episodios registrados en agosto.

Sostuvo que se cumplió el desafío de la alerta sanitaria en cuanto a disminuir el efecto de las emisiones sobre los casos con sintomatología compatible a intoxicación ya que durante esta última semana, prácticamente, no hubo consultas asociadas a este tema.

Expresó que las tres cuartas partes de los afectados se atendieron en el Hospital de Quintero, y el resto se enfocó principalmente en la atención primaria tanto del Cesfam de Puchuncaví en el Cesfam de Ventanas, y en la posta de Loncura.

Respecto de la distribución etaria, destacó que casi la mitad de los casos correspondió a niños, niñas y adolescentes entre 10 a 19 años, y el resto de los afectados en los otros rangos etarios.

Resaltó que la sintomatología que presentaban era cefalea, nauseas, vómitos, dolor abdominal, cólicos, mareos, y en menor medida síntomas como parestesia, hiperreflexia, etcétera. De ello quienes presentaron sintomatologías como parestesia o hiperreflexia, fueron derivados a interconsultas por especialistas y además se les hizo encuestas domiciliarias.

En cuanto a la salud mental explicó que se inició una mesa regional con la participación de la Seremi de Salud, el director de la Onemi, los seremi de Desarrollo Social, de Cultura, de Educación, la Junji, Junaeb, Integra, Injuv y los

municipios de Quintero y de Puchuncaví, con reuniones periódicas para elaborar un plan de trabajo y el 21 de septiembre difundieron un documento “Consideraciones Generales para la Comunidad Educativa en el Retorno a Clases en las comunas de Quintero y de Puchuncaví” para preparar y planificar el retorno a clases de los estudiantes de la zona.

Otra de las estrategias fue coordinar la Red de Salud Mental tanto a nivel de atención primaria como a nivel de especialidad, en que el Servicio de Salud Viña del Mar-Quillota estableció un flujo de derivación y atención expedito e inmediato para las personas que estaban consultando.

También se capacitación para ayuda sicológica y se realizaron jornadas para más de 50 profesionales del Ministerio de Salud, Onemi, Seremías de Salud, de Desarrollo Social, de la Mujer, servicios de Salud, Junji, Municipalidad de Puchuncaví, posta de Loncura, Cesfam de Ventanas y el hospital de Quintero.

Igualmente se desplegó un equipo de respuesta rápida cuya primera ayuda la entregó a los funcionarios que estaban trabajando y realizando la atención de todos los pacientes que llegaron al hospital de Quintero.

En relación con el ámbito de educación y comunicación de riesgo, precisó que se han realizado 4 talleres de educación sanitaria ambiental dirigidos a 44 directivos de establecimientos educacionales de Quintero; a 46 directivos de establecimientos educacionales de Puchuncaví; a 16 asistentes de centros de padres y apoderados; y a 23 asistentes entre padres, apoderados y centro de alumnos de Puchuncaví.

Por otra parte, sostuvo que la alerta sanitaria le permitió como seremi de Salud ampliar el ámbito de fiscalización y establecer un control estricto de la disminución de emisiones de contaminantes, y de esa forma disminuir el impacto en la población.

Comentó que a partir de la dictación del decreto el 27 de septiembre hubo una paralización parcial Codelco Ventanas detuvo 3 de los 9 ciclos de operación diaria, reduciendo así en un tercio sus emisiones. Por su parte, AES Gener deberá detuvo completamente su unidad generadora número 1, la más antigua y contaminante del complejo. Respecto a las fuentes generadoras de compuestos orgánicos volátiles en las empresas del sector de hidrocarburos, se determinó que las empresas Oxiquim, Copec, Gasmar, ENAP Quintero, Enex y GNL Quintero, deberán paralizar las algunas actividades o fuentes de emisiones.

También se solicitó a 13 empresas del complejo industrial presentar planes operacionales, lo que significó que las empresas se comprometieran a bajar las emisiones para disminuir la contaminación ambiental y todos los días las empresas envían un reporte que ayuda a vigilar que se cumplan los compromisos establecidos en los planes operacionales. Señaló que se encuentran en una segunda revisión de los planos operacionales para así afinar algunos procesos y analizar si es posible exigir un poco más a las empresas en cuanto a algunos procesos. Hay una evaluación técnica-jurídica para que las medidas de reducción de emisiones implementadas por los planes operacionales de cada empresa puedan ser permanentes, luego de levantada la Alerta Sanitaria.

Agregó que se han realizado 417 fiscalizaciones, algunas en conjunto con la Superintendencia del Medio Ambiente y otra con la Superintendencia de Electricidad y Combustible y que han clasificado a las empresas según la cantidad emisiones que emiten. Así en el grupo 1 están las empresas que emiten compuestos orgánicos volátiles, como ENAP, Oxiquim, Copec TPI, Copec Lubricantes, Gasmar y Enex; en el grupo 2 están aquellas empresas que emiten dióxido de azufre y material particulado, como Codelco, Aes Gener, Enel y GNL Quintero, y en el grupo 3 están las empresas que emiten varios contaminantes, como Cemento Melón, Pesquera Quintero, Puerto Ventanas y Catamutun.

Finalizó diciendo que la declaración de alerta sanitaria es histórica y un ejemplo a nivel mundial respecto de cómo controlar rápidamente las emisiones de las empresas.

5.- SEÑOR MARCELO FERNÁNDEZ, JEFE DE LA DIVISIÓN DE CALIDAD DEL AIRE Y CAMBIO CLIMÁTICO DEL MINISTERIO DEL MEDIO AMBIENTE.

Sostuvo que la zona de Quintero y Puchuncaví tuvo efectos favorables con la implementación de dos normas de emisión: una de ellas, la de termoeléctricas, publicada en 2011 y que entró en plena vigencia en la zona en junio de 2015. La otra es el decreto N° 28, la que se refiere a la norma de fundiciones de cobre, publicada en 2013 y que entró plenamente en vigencia a partir de diciembre de 2016.

Recordó que la zona fue declarada saturada en el año 2015 por PM 2,5 y que se elaboró un plan, que fue representado por la Contraloría en diciembre de 2017. Agregó que asumió el cargo de jefe de la División de Calidad del Aire y Cambio Climático del Ministerio del Medio Ambiente, en marzo de 2018.

Mencionó que en Chile la norma de calidad del aire para dióxido de azufre está obsoleta pues hace mucho tiempo que no ha sido actualizada.

Un aspecto muy complejo de la zona, se produce con el monitoreo de calidad del aire, toda vez que la supervisión se encuentra bajo la tutela de las empresas. Explicó lo anterior, indicando que las empresas productoras de las emisiones contaminantes son las mismas encargadas de medir la calidad del aire, por lo tanto, se generó un tema complejo sobre todo respecto de la credibilidad de la comunidad.

Indico que después de los eventos de agosto y septiembre pasado se generó un escenario distinto para el nuevo plan de descontaminación y por eso consideró aspectos que el anterior no contenía como la emisión de hidrocarburos.

Advirtió que otro tema fundamental, a propósito de la crisis, se refiere a la mala ventilación de la bahía, así durante la noche y particularmente en el invierno, la ventilación de la zona costera entre Concón y Quintero es muy adversa, lo que provocó las condiciones necesarias para la acumulación de contaminantes y la ocurrencia de episodios críticos ya que la contaminación se acumuló y, en consecuencia, se produjeron *peaks* muy altos de dióxido de azufre.

Explicó que a partir de estos hechos se ha realizado planteado una nueva estrategia de gestión de la calidad del aire para la zona. El monitoreo de la calidad del aire tiene que estar bajo la supervisión del Estado, y se rediseñará para transformarla en una red con altos estándares de control y aseguramiento de calidad

de los datos, lo que permitirá realizar las mediciones de contaminantes que actualmente no han sido medidos, además de implementar un estándar más exigente.

Informó que también se están tomando medidas para sacar adelante la norma primaria de la calidad del aire para SO_2 con un límite de una hora. Señaló que la norma fue presentada al Consejo de Ministros en la administración anterior, la que fue aprobada por todos excepto por la Ministra de Salud de la época. Se comprometió a efectuar la revisión correspondiente e ingresarla a la Contraloría antes del 31 de diciembre de 2018.

Sobre la alerta sanitaria, expresó que es un instrumento que fue definido en conjunto con el Ministerio de Salud para hacer frente a la crisis entre el período del 25 de septiembre, fecha en que entró en vigencia, hasta que el plan de descontaminación sea publicado. Agregó que el objetivo es realizar todos los días las mediciones correspondientes en la zona, lo que definitiva implica que la alerta sanitaria culminará con la puesta en marcha del plan de descontaminación.

Acerca de las diferencias entre el plan de descontaminación anterior fallido y el nuevo, sostuvo que recae en los niveles de material particular de 2,5, toda vez que es el contaminante principal de la zona, las emisiones se reducen hasta quedar por debajo del nivel de latencia y, por lo tanto, en pleno cumplimiento de las normas. Explicó que para lograr esa reducción de emisiones se estableció reducciones de material particulado, dióxido de azufre y óxido de nitrógeno, junto con agregar hidrocarburos, los que no estuvieron en forma tan clara en el plan anterior. Sostuvo que, también se establecen exigencias mayores respecto de los graneles sólidos y áridos. Agregó que las empresas tuvieron que hacer inversiones importantes para cambiar la forma en que actualmente maneja el carbón a nivel de graneles, por las emisiones que se producen en la zona.

Este plan de descontaminación establecerá diversos instrumentos tales como límites de emisión anual más exigentes para las fuentes existentes, medidas de control de emisiones de hidrocarburos, gestión de episodios críticos, entre otros. Se establecieron ciertas exigencias permanentes durante el período abril a septiembre, además, de aquellas exigencias que no permanentes, que estarían asociadas a pronósticos el resto del año, es decir, durante todo el año se tendrá la posibilidad de reducir emisiones en forma adicional para efectos de reducir los impactos asociados a la mala ventilación. Explicó que el pronóstico de mala ventilación se ha ido haciendo desde el mes septiembre. Además, mostró el máximo de dióxido de azufre en todas las estaciones de Quintero y Puchuncaví. Junto con ello, comparó el estándar chileno con el estándar de la Unión Europea de una hora, para ponerlo como referencia.

En síntesis resaltó que, los aspectos diferenciadores del nuevo plan de descontaminación, dicen relación con el control de hidrocarburos y el plan de gestión de episodios críticos.

Evidenció que a partir del 25 de septiembre, fecha en que partió la alerta sanitaria, los niveles de una hora se fueron reduciendo en forma significativa, llegando, incluso, a estar muy por debajo de lo que estableció la Unión Europea como estándar de una hora en la mayor parte de los días y de las horas. Sostuvo la evidente necesidad de fortalecer la alerta sanitaria en el tiempo y mantenerla como mecanismo de gestión de episodios críticos.

Sostuvo que un efecto para la zona de las medidas adoptadas ha sido que, a partir de octubre, el número de atenciones de salud y problemas relacionados han bajado en forma muy significativa.

Consultado por las razones por las que el nuevo plan de descontaminación es exigente con ENAP y Codelco para bajar los niveles de dióxido de azufre, óxido de nitrógeno y de material particulado, no obstante, ser laxo con AES Gener, indicó que no se efectuó dicha distinción, toda vez que lo que se realizó fue reconocer las emisiones permitidas en cada industria. Ejemplificó señalando que en el caso de Codelco Ventanas se encontraban en la norma que entró en vigencia plenamente en diciembre de 2016, teniendo 14.650 toneladas permitidas, mientras que 1.000 toneladas permitidas de material particulado, correspondiendo aquello a una exigencia muy antigua, que data del plan de descontaminación de 1992.

Explicó que lo primero que se hizo fue congelar las emisiones, lo que significa que si la industria efectuó un esfuerzo de reducción por debajo de lo que tiene permitido, el excedente se le quita de forma inmediata con la publicación del plan. Sostuvo que la razón de quitar ese excedente es simplemente para asegurarse de que no vuelva atrás ni en una sola tonelada, motivo por el cual desde el primer día en que se publicó el plan, las emisiones bajaron. Sostuvo que a las empresas se les exigió una reducción total del 35% de azufre o de dióxido de azufre y 95% de reducción del material particulado.

Señaló que en el caso de AES. Gener Ventanas, el material particulado se encontraba muy por debajo de lo permitido, emitiendo alrededor de 25% de lo permitido; lo mismo para el dióxido de azufre y sus emisiones de óxido de nitrógeno.

Producto de ello al momento de calcular las reducciones, se puede apreciar una suerte de favorecimiento, no obstante, desde la entrada en vigencia del plan, se eliminó completamente todo el excedente, es decir, toda reducción que se generó, quedó prohibida a partir de ese momento, mientras que el nuevo límite, denominado congelamiento, se estableció considerando el promedio de los últimos dos años en los que la industria había dado cumplimiento a la norma.

Indicó que a las termoeléctricas se le exigieron límites en chimenea específicos para material particulado, además, las dos chimeneas que tenían un límite de 20 se mantuvieron, mientras que, aquellas que tenían un límite de 50, se bajaron a 20 en material particulado. Sostuvo que la norma establece 50 miligramos para todas las unidades. Sin embargo, cuando la central Gener pasó por el SEIA, le establecieron exigencias mayores en cuanto al límite más bajo a las unidades 1 y 2, además de establecer mayores exigencias a las unidades 3 y 4, es decir, 20.

Declaró que para la última de las tres grandes industrias que emitieron el 80% de todas las emisiones, ENAP Aconcagua el plan era mucho más exigente, toda vez que no se tuvo ningún cumplimiento de norma previa, al no estar sometidas a un proceso de regulación. Advirtió que no se tuvo ni siquiera emisiones permitidas, producto de la ausencia de normas, exceptuando al dióxido de azufre, que en su Resolución de Calificación Ambiental, tenía establecido un límite de 2.190 toneladas. Señaló que se emitieron 1.492 toneladas, motivo por el cual se decidió congelar. Explicó que el valor de congelamiento, en el caso de ENAP, no se produce después de cumplir una norma, porque no la tiene, sino que el congelamiento se realizó en función del promedio de los últimos tres años.

Preguntado si existe algún plan o reflexión sobre la medición de la calidad del aire en las zonas de sacrificio en general, precisó que tratándose de las zonas industriales el Estado debió supervisar las estaciones de calidad del aire, sin que ello signifique que las financie. Señaló que para llevar a cabo lo anterior, es necesario rediseñar las redes y hacer exigencias de redes nuevas de monitoreo a las industrias que sean supervisadas por el Estado. Agregó la importancia de en estas zonas mantener el principio responsabilidad a todo aquel que contamina, en otras palabras, todo aquel que contamine debe pagar.

Sobre la máxima concentración de dióxido de azufre que permitirá la norma en el nuevo plan de descontaminación, respondió que se van a medir los mismos contaminantes, pero con criterios actuales, y que consiste en regular las emisiones contaminantes -principalmente material particulado (MP 2,5 y MP 10) y el control de emisión de gases volátiles que actualmente no cuentan con regulación

Se refirió a las fuentes sin Resolución de Calificación Ambiental, indicando que una de las ventajas del plan de descontaminación son las restricciones impuestas a las empresas que ingresan al Parque. Además permite que las fuentes que ya se encuentran instaladas en la zona sean fiscalizadas de mejor forma, pese a no contar con una Resolución de Calificación Ambiental.

6.-SEÑORA JAVIERA OLIVARES, JEFA DE LA DIVISIÓN DE EDUCACIÓN AMBIENTAL Y PARTICIPACIÓN CIUDADANA MINISTERIO DE MEDIO AMBIENTE.

Indicó que tuvo que asumir la responsabilidad de llevar a cabo el proceso de participación ciudadana del Plan de Prevención y Descontaminación Atmosférica de Quintero, Concón y Puchuncaví, que se dio en un contexto abreviado, porque este es un plan que se sometió con urgencia y el proceso se redujo a treinta días hábiles, para desarrollar todas las actividades participativas y también recopilar las distintas observaciones ciudadanas que han llegado al Ministerio.

Mencionó que este proceso conllevó un esfuerzo grande, por parte del Ministerio, en materia de organizar, planificar y garantizar la mayor cantidad de espacios posibles, a los efectos de desarrollar actividades presenciales donde pudiesen llegar personas representativas de la comunidad.

Informó que en cuanto a las actividades presenciales, se desarrollaron dos tipos de metodologías: diálogos participativos y casas abiertas. La idea fue llegar con metodologías acordes a la realidad local y a las particularidades de cada una de las comunas, con amplitud horaria, para garantizar la asistencia de todas aquellas personas que quisieran participar del proceso.

Comentó que respecto de las instancias de participación ciudadana que conlleva un plan de descontaminación de estas características, el acceso a la información relevante, que tiene que ver con la OIRS, el sitio *web*, las llamadas telefónicas, las oficinas de parte que siempre están a disposición en el Ministerio de Medio Ambiente; la recepción de antecedentes técnicos, que se desarrolló del 3 al 18 de octubre de 2018 -tienen que ver con la recepción de antecedentes técnicos para elaborar el anteproyecto del plan de descontaminación-; el proceso de consulta ciudadana que está relacionado con los 30 días hábiles y con un plan de participación ciudadana bien exigido, y la opinión de los consejos consultivos a nivel nacional y regional.

Relató que en esta zona también está operando el CRAS, Consejo para la Recuperación Ambiental y Social de Quintero y Puchuncaví, quienes también ayudaron a diseñar y modelar los procesos de participación y las actividades presenciales que desarrollaron.

Precisó que el 22 de octubre el subsecretario del Medio Ambiente y el Intendente se reunieron con los alcaldes y concejales de las comunas de Concón, Quintero y Puchuncaví, y con los representantes del Consejo de Recuperación Ambiental y Social de la zona para detallar el proceso de participación ciudadana del plan de prevención y descontaminación atmosférica para estas tres comunas. Indicó que en este mismo contexto se realizó un despliegue territorial, que comenzó el lunes 29 de octubre, donde se entregó información para la participación ciudadana respecto del lugar dónde se iban a realizar cada una de las actividades, los horarios, los mecanismos de transportes, etcétera, para facilitar la participación de la comunidad. Ese día recorrieron las localidades de Santa Adela, Santa Julia, Mantagua, San Ramón, Santa Luisa, Santa Rosa de Colmo, Loncura, Valle Alegre y Ritoque. Cada una de estas actividades tuvo un despliegue presencial de funcionarios del Ministerio de Medio Ambiente y de la Intendencia. Para efectos de garantizar la correcta información de las personas, el criterio fue que siempre fuese alguien del Ministerio de Medio Ambiente para poder zanjar ciertas dudas técnicas que pudiese la comunidad tener. Los mismos criterios se utilizaron el día martes 30 de octubre en las localidades de Puchuncaví y Concón.

El día miércoles 31 de octubre se reforzó la convocatoria y se recorrió nuevamente Puchuncaví, Concón y Quintero con un tremendo esfuerzo del equipo del Ministerio de Medio Ambiente, que recorrieron cada una de las localidades, pegando afiches y haciendo puerta a puerta en las comunidades más alejadas o rurales, como es el caso de Puchuncaví, para garantizar la participación ciudadana.

Respecto del material gráfico que se entregó, indicó que fueron 4.000 trípticos con información sobre el anteproyecto y sus medidas; 10.000 volantes, 500 afiches, y 3 pasacalles, uno para cada una de las comunas en consulta.

Declaró que para garantizar la convocatoria se llevó a cabo difusión y se contrató a tres radios locales: Radio Interferencia, Radio Nueva Puchuncaví y Radio Loncura. Se dispuso para la comunidad servicios de transporte especial para asistir a las actividades, se contactó directamente a los tres alcaldes y se expuso el calendario y la metodología de trabajo en el Consejo para la Recuperación Ambiental y Social de Quintero y Puchuncaví (CRAS).

En resumen, fueron 9 las actividades de participación ciudadanas. Estas consistieron en 5 diálogos participativos y 3 casas abiertas y en la última actividad contaron con la participación y con la exposición de quien está a cargo de este plan en materias técnicas, que es el jefe de la División de Calidad de Aire del Ministerio de Medio Ambiente.

En los diálogos participativos contaron con 262 personas, en casas abiertas con 39 personas, y en el colegio General Velázquez de Puchuncaví con 130 alumnos, lo que da un total de 431 participantes.

Luego, abordó las observaciones que se pudieron obtener de las actividades presenciales, entre ellas:

1.- Cuestionamientos al carácter no vinculante del proceso de participación ciudadana.

2.- Inquietud sobre las causas y responsabilidades por los eventos contaminantes ocurridos en agosto.

3.- Preocupación por la autonomía y rediseño de la red de monitoreo de la calidad atmosférica.

4.- Mayor transparencia y claridad en la fiscalización. Quinto, la necesidad de extender el plan de descontaminación a otros componentes ambientales, como agua, suelo, etcétera.

Concluyó, afirmando que en el proceso formal recibieron 777 observaciones de 243 observadores, personas naturales y jurídicas y que el proceso se terminó el viernes 14 de diciembre de 2018 y que se encuentran en periodo de sistematización y de análisis técnico de la División de la Calidad del Aire y de la División Jurídica.

7.- SEÑOR JORGE MARTÍNEZ, INTENDENTE DE LA REGIÓN DE VALPARAÍSO.

Expresó que luego de los episodios del 21 y 23 de agosto; 4 de septiembre y 24 de septiembre, se decreta alerta amarilla en el territorio el jueves 23 de agosto, que se levantó el 1 de septiembre para retomar las clases, y se interrumpe por un nuevo episodio el día 4 de septiembre, retomándose y levantándose la alerta amarilla el 20 de septiembre.

Luego, el 27 de septiembre se dicta el decreto supremo que estableció la alerta sanitaria en el territorio. Agregó que este es un decreto supremo histórico, que nunca se había dado en el territorio, y que es sumamente restrictivo para las tareas que las diecisiete o diecinueve empresas que están ubicadas en ese cordón industrial pueden y deben realizar a partir de ese minuto. En efecto todas las empresas ven reducidas sus actividades y se les pide elaborar un plan de manejo de operaciones para reducir sus emisiones de contaminantes, aun estando permitidas. Esos planes de reducción de operaciones son sometidos a estudios por los Ministerios de Salud y del Medio Ambiente, los que hacen modificaciones, precisiones y restricciones a determinadas faenas, y una vez que son autorizados pueden volver a operar esas plantas.

Junto con eso, este decreto supremo de alerta sanitaria se dicta también en forma inédita el 4 de octubre la alerta preventiva que opera del mismo modo -o muy similar- a la forma en que opera la restricción ambiental en Santiago cuando se decreta preemergencia.

Señaló que entiende -por las actas de sesiones anteriores- que se ha encontrado una relación de causalidad entre la inversión térmica que se produce, sobre todo en las noches, en la bahía de Quintero, la situación medioambiental, con los episodios de contaminación incluso dentro de las emisiones permitidas a las empresas que están en el territorio.

Entonces todos los días la Dirección de Calidad del Aire del Ministerio del Medio Ambiente, en conjunto con la Dirección Meteorológica de Chile, envía a la intendencia regional un pronóstico de calidad del aire o de las condiciones ambientales para las próximas 24 horas.

Si ese pronóstico establece que va a haber malas condiciones ambientales, por tanto, los gases no se van a diluir o no se van a mover de ese territorio, el Seremi de Salud emite este decreto de alerta preventiva que obliga a todas las empresas que tienen planes operativos autorizados a bajar las emisiones hasta el plan operativo autorizado, y aquellas que no tienen plan operativo se reducen hasta las restricciones que se les impusieron con el decreto supremo de alerta sanitaria.

Este sistema lleva más de un mes de operación, y es de público conocimiento que han existido muy pocos casos de personas con síntomas de intoxicación en los hospitales, llegando a una situación que podrían llamar de bastante normalidad. Incluso, habiendo actividades normales como la que hubo este fin de semana con las festividades que se hicieron en la bahía de Quintero.

Agregó que el 31 de octubre pasado se publicó en el Diario Oficial el anteproyecto de descontaminación ambiental de Quintero, Puchuncaví y Concón, anteproyecto que tuvo un plazo para entregar informe y estudio, y a partir de hoy comienza el plazo para la participación ciudadana y hasta el 14 de diciembre. En este lapso se van a generar en el territorio diálogos participativos, casas abiertas, que han sido ampliamente difundidas en toda la población mediante diversas folleterías, avisos en los medios de comunicación, etcétera, para que la población de Quintero, Puchuncaví y Concón pueda participar y realizar aportes. El 14 de diciembre se recogen todos los aportes, los estudios y se elabora el plan de descontaminación de Quintero y Puchuncaví, que el Presidente de la República se ha propuesto ingresar a la Contraloría General de la República a más tardar el 31 de diciembre próximo.

Adujo que le parece muy relevante contar que dentro de este mismo proceso se ha dado a conocer un convenio suscrito por el Ministerio del Medio Ambiente con el Instituto Noruego de Investigación del Aire, NILU, que es el más prestigioso Centro de Calidad del Aire de Europa y que va a poner a disposición sus instalaciones, sus profesionales, que ya están en el territorio, y tecnología de punta.

En concreto, el equipo NILU, que está liderado por el doctor Norbert Schmidbauer, va a tomar en estos días -ya partieron revisando el territorio este fin de semana- doscientas muestras de aire en la zona Quintero, Puchuncaví y Concón, las que van a permitir obtener, mediante un sistema bastante especial que se ocupa en Europa el *fingerprint* –huella digital- de todos los contaminantes de la zona.

Un tema importante en materia ambiental es el principio de que la concentración hace el veneno. Es decir, no es solamente encontrar o no un compuesto en el aire, que probablemente uno encuentre de todo en el aire, sino que la cantidad es lo peligroso para la población y la fuente emisora.

Por lo tanto, con estas muestras que se van a Noruega para ser examinadas, porque allá está la tecnología, a fines de enero se va a tener el análisis completo y la huella digital completa del aire que se registra, de las condiciones del aire y contaminación en las comunas en cuestión.

El gobierno también ha anunciado la creación de un laboratorio de alta complejidad, a nivel nacional, con el apoyo de este instituto noruego. Recordó que la modernización del sistema de monitoreo es asesorada por el gobierno de Finlandia, porque se están buscando los mejores referentes a nivel mundial para ambos temas. La idea es que este laboratorio, con certificación internacional y de alta complejidad,

sea construido desde principios del próximo año. Este laboratorio no solo permitirá medir compuestos aéreos, sino también en el suelo, agua y en residuos. Será un laboratorio de referencia para todo el país.

De manera, señaló que después de un período que ha sido bastante intenso el gobierno sigue cumpliendo su palabra de generar un antes y un después. Con todas estas medidas, esperan nunca más, en las zonas de Concón, Quintero y Puchuncaví, se tenga que lamentar episodios de contaminación como los vividos durante 54 años.

Acto seguido, al responder diversas consultas de varios señores diputados, precisó que desde el 21 de agosto hasta el 21 de octubre, durante dos meses, había tenido alrededor de 140 reuniones, con todo tipo de organizaciones comunitarias, incluyendo pescadores, asociaciones gremiales, pequeños comerciantes, artesanos, padres y apoderados, uniones comunales y juntas de vecinos; por cierto, con los tres concejos, con los tres alcaldes y con clubes deportivos, entre otros. Sostuvo que prácticamente, se ha reunido con todas las organizaciones vivas y representativas de distintas instancias de las tres comunas.

Precisó que de las conversaciones con todas las comunidades recogió varias conclusiones. Primero, el dolor histórico de algunos; segundo, la resignación de otros, que piensan que esto es así y que no va a cambiar nunca; y tercero, y aclaró que puede dar fe de ello y remitirlo a las organizaciones con las cuales conversó, de que la inmensa mayoría de las organizaciones con las que se reunieron al aire libre, en un cabildo abierto -salvo dos o tres excepciones muy particulares- no quería que las empresas se fueran, solo quieren que no causen daño. Ellos entienden que si las empresas se van, pierden fuentes de trabajo, pierden parte de su futuro; quedar estigmatizados como zona de sacrificio es algo que les complicaba mucho. Ellos quieren, de verdad, que las empresas no contaminen, y ellos les han dicho que van a elaborar un plan, justamente enfocado a no contaminar.

El plan de descontaminación está diseñado a 5 años, como la mayoría de estos planes, con un límite en los próximos 3 años. Es un plan que se centra en dos tipos de medidas: estructurales y de gestión de episodios críticos.

Las medidas estructurales parten de una realidad. En cuanto a emisión de toneladas por año, las tres fuentes principales de la zona, como son Enap, Codelco y Aes Gener, representan 75 por ciento del material particulado de todo el territorio; representan el 99 por ciento del dióxido de azufre de todo el territorio y el 81 por ciento de todos los óxidos de nitrógeno de todo el territorio. Es decir, habrá restricciones para todos, porque el plan es para todas las empresas, sean públicas o privadas, no hay distinción, pero se pone énfasis en tres, tal como lo considera el plan, y con eso se reducen significativamente las emisiones.

En resumen, mediante este plan, en Codelco se rebajan 95 por ciento de las emisiones de material particulado de la cifra permitida; se rebaja 35 por ciento de las emisiones de dióxido de azufre; en Aes Gener, se rebajan 75 por ciento de las emisiones de material particulado, 40 por ciento de dióxido de azufre y 32 por ciento de óxidos de nitrógeno; y en Enap, que no tiene los mismos componentes, se reduce 75 por ciento de material particulado y 40 por ciento de dióxido de azufre, sin perjuicio de las medidas que se están adoptando, que son parte del plan para ciertas sustancias que aún no están normadas. Si no existe norma para establecer una disminución hay que tener una línea base, línea que se construye en tres años.

Agregó que al incorporar el laboratorio -el mejor instituto del mundo en mediciones de contaminantes de suelo, aire o agua-, probablemente -y este es un supuesto-, va a permitir determinar la existencia de muchos gases y, en la medida en que esos gases sean perniciosos para la salud o para el medio ambiente -porque se va a poder establecer el tipo, la fuente y la cantidad-, y así las normas que permitan la reducción.

Sostuvo que con la sola entrada en vigencia del plan de descontaminación se produce una gran disminución de las emisiones, porque se les pone como techo a las empresas el promedio de los tres últimos años que, por cierto, es más bajo que el total autorizado a cada empresa. Lo explicó con el siguiente ejemplo: si Codelco tiene en emisiones de SO2 permitido, 14.650 toneladas al año, solo con la vigencia del plan, considerando el promedio de los tres últimos años, baja a 10.561; o sea, disminuye 4.000 toneladas por la sola entrada en vigencia del plan, llegando al 1 de enero del tercer año a 9.500 toneladas, que es una reducción de 35 por ciento de SO2, en el caso de Codelco.

Insistió que el plan tiene medidas de tipo estructural, que pretenden abarcar todas las empresas de la zona; y que se espera congelar las emisiones al promedio o a la norma que se permitía, si es que esta es la que corresponde, y, a partir de eso, iniciar un plan de reducción en forma importante. Agregó que lo más probable era que en este periodo se pudieran establecer normas respecto de sustancias no normadas, como los COVs, los compuestos orgánicos volátiles, para los que no existe normativa. Pero con estas mediciones ciertas, objetivas, científicas, se podrán establecer criterios para hacer rebajas y asegurar en todo ese sector que no exista peligro de contaminación.

Respecto de metales pesados, indicó que no existe normativa. Entonces, con esas mediciones, se podrán construir las líneas bases, para lo que se requiere tiempo, y de esa manera establecer una normativa para todas aquellas sustancias que contaminan.

En cuanto a los indicadores a símiles internacionales, sostuvo que el gobierno estaba trabajando con Noruega, con el mejor organismo técnico en el tema, y con el gobierno de Finlandia, para diversos temas de monitores. Agregó que los finlandeses son los que tienen los mejores estándares europeos al respecto, y esos son los que quieren aplicar en el territorio.

En relación con el polen, efectivamente, el primer episodio partió el día martes 21 de agosto; el día jueves 23, muy temprano en la mañana, empezó a aparecer en las redes sociales mucha información errónea que comenzó a causar alarma temprana en la población, porque se comentaba que había arsénico en todas partes, arsénico que se expandía desde Puchuncaví hasta Laguna Verde. Se trataba de una mezcla de agua con un color amarillento y con algo blanco, que estaba más concentrado, incluso en la zona de Concón, en los altos de Viña y de Valparaíso, llegando hasta Laguna Verde. La alarma, dada por personas líderes de opinión, era que había contaminación por arsénico en el territorio y que el gobierno no hacía nada.

Se ordenó de inmediato tomar muestras; incluso, agregó, que tiene los certificados de los laboratorios del Servicio de Salud que demuestran que se trataba de polen, un fenómeno que ocurre cada cierto tiempo en la zona y que por la dirección del viento, por una llovizna que hubo esa mañana de vaguada costera, generó esas condiciones.

Alguien podrá discutir los resultados de los laboratorios del servicio de Salud, pero los laboratorios de la Universidad Católica en Curauma, los laboratorios de la Universidad de Valparaíso y otro laboratorio independiente, confirmaron que se trataba de polen. Destacó que en esta situación lo importante es dar certeza a la comunidad y no alarmarla innecesariamente. Eso es muy dañino para la población, por eso sintió la obligación de decir lo que después se confirmó: que lo que se encontró en el territorio era efectivamente polen, certificado por laboratorios especializados anteriormente señalados.

Respecto de la información de datos erróneos, algunos parlamentarios, entre ellos el senador Chahuán, presentaron una querella contra quienes resultaran responsables por la contaminación. Dentro de sus considerandos se invocaba un informe de la Seremi de Salud que indicaba una concentración de SO2, de 750 milimilígramos por metro cúbico, información que no concordaba con la realidad, por lo que ordenó investigar en la Seremi, y efectivamente una persona que ya no trabaja en la institución porque fue desvinculada, al transcribir un informe y poner 75,4 puso 754.

En cuanto a la razón de no paralizar todas las faenas, indicó que hay un antecedente jurídico y que se da en relación al recurso de protección presentado ante la Corte de Apelaciones de Valparaíso, solicitando la paralización del cordón industrial de Quintero-Puchuncaví por los efectos de la contaminación al que la Corte no dio lugar por carecer de individualización el autor de la contaminación.

Lo resuelto por la Corte se aplica a la razón de no paralizar todas las faenas pues no se puede identificar al causante ni a la fuente emisora, clara y precisa que al no tener absoluta certeza jurídica de cuál era la fuente directa o causante de la contaminación, no se puede paralizar a todos. .

Sin perjuicio de ello, y a raíz del principio de la prevención en materia ambiental la sola sospecha de que algún contaminante esté dañando a la población permite tomar medidas y en ese sentido se dictó la alerta amarilla, la alerta sanitaria y adoptar distintas medidas como la reducción de emisiones a todas esas empresas en forma inmediata. Así es cómo se ha ido logrando que los casos se reduzcan; prácticamente, en los últimos 30 días, en 24 o 25 días, han ordenado a las empresas reducir sus faenas a su plan operativo o a las condiciones que generaron en el decreto de alerta sanitaria.

En cuanto a la central de Concón, hay que ser muy respetuosos de los procesos que se siguen conforme a derecho. Hay una planta aprobada por la RCA para desalinizar agua en Quintero. Incluso, dijo que se consultó a las comunidades y respondieron que esa planta no contamina y como hay sequía, estuvieron de acuerdo.

Indicó que respecto al área de extensión del Premval, se reunieron con los alcaldes de Quintero y de Puchuncaví, con los Consejeros Regionales, con el Presidente del Consejo Regional y con la agrupación o Comité de Consejeros Regionales de la zona norte de Valparaíso, quienes les han dicho que hay, según el Premval, un área en la que se podrían instalar empresas contaminantes, aproximadamente 500 hectáreas. Al respecto, han llegado a un acuerdo preliminar, porque esto también tiene un proceso que está reglado y deben asumirlo, para congelar esas 500 hectáreas. Aunque existen distintas alternativas que se están evaluando, además, acotó, quieren escuchar a la comunidad para saber si tienen interés en otro tipo de actividades, en la medida que no sean contaminantes o, como

han pedido algunas organizaciones, que sea un área destinada a un parque o a áreas verdes. En lo que sí están de acuerdo con el consejo regional es en iniciar el proceso –en lo que a ellos respecta de la regulación del Premval- y hacer las modificaciones para que no se instalen empresas contaminantes en el sector.

En relación con la solicitud de ampliación de concesión marítima, precisó que la Comisión de Borde Costero no tiene carácter vinculante, sino que es una opinión ciudadana, es parte del proceso de participación ciudadana, porque finalmente resuelve el Subsecretario de las Fuerzas Armadas, teniendo a la vista distintas opiniones. Agregó que los participantes en la Comisión son cerca de sesenta. Se encuentran alcaldes, seremis, entre muchas autoridades del mundo social. Agregó que cuando se discutió esta ampliación venía con un informe favorable y en la discusión no se objetó ya que no contenía ningún elemento que se pudiera objetar.

Lo único que se mencionó, y que le gustaría que se aclarara, es que al finalizar la votación del proyecto -que tiene RCA- a mano alzada –por eso no están en el acta los nombres de cada uno-, el consejero Crichton comentó que iba a presentar un recurso sobre la ilegalidad de dicho procedimiento, ante lo cual le manifestó que estaba en su derecho y que le parecía muy correcto si es que había algo ilegal, pero el secretario técnico y el equipo señalaron que cualquier observación respecto de la tabla de ese día se tenía que comunicar con 24 horas de anticipación.

Sobre los tres grandes temas que el Presidente de la República les encomendó en los primeros días de la crisis fueron los siguientes:

Primero, la salud de la población. Era el primer tema y ahí vino el hospital especial, el PAME (*Puesto Avanzado de Médicos Especialistas*), el apoyo de la Fuerzas Armadas, la llegada de especialistas y muchas medidas que se tomaron para dar seguridad en materia de salud a la población.

Lo segundo, tomar medidas para que no se siguieran produciendo episodios de contaminación que alteraran la salud de la población.

Lo tercero, gran parte de las reuniones previas a fiestas patrias y con posterioridad a ellas, dado que es una comunidad que tiene una economía bastante débil que depende mucho del comercio menor y de la actividad turística propia del sector por lo que cuadriplica sus habitantes en el verano, trataron acerca del justo temor que ellos sentían a que por ser estigmatizados como zona de sacrificio no tuvieran –ya habían perdido las fiestas patrias- verano. En razón a eso y a las reuniones con todas las organizaciones de turismo, de comercio y organizaciones sociales, en conjunto con el gobierno regional y con el Ministerio de Economía, se acordó adoptar un paquete de medidas que involucran la aplicación de los distintos instrumentos de los que dispone el Estado. Ya se aplicó uno este fin de semana con Sercotec -el pescado más largo- y se ha programado realizar una serie de distintas actividades, algunas culturales. En total, se acordó aplicar un conjunto de medidas cuyo costo es cercano a los 2.800 millones de pesos, gran parte a ejecutar en los meses de noviembre y diciembre para que los pequeños comerciantes, los artesanos los vendedores ambulantes, y una gran cantidad de personas que ha visto mermadas sus ingresos en este periodo puedan estar preparados dado que necesitan material para poder enfrentar la temporada estival bien y, además, otros, para poder potenciar el turismo en sus localidades en forma efectiva.

De ese paquete de 2.800 millones de pesos una parte -casi la mitad- la aporta el Ministerio de Economía a través de sus distintos brazos, como Corfo y Sercotec, y la otra mitad la pone el gobierno regional.

A los demás ciudadanos afectados por este proceso de contaminación que ha sido tan doloroso, para los estudiantes, los adultos mayores y para todos -pues es un proceso que a todos ha afectado-, se les ha garantizado desde el primer minuto la protección de la salud de las personas y han tomado todas las medidas para dar las condiciones necesarias del mejor nivel, con toxicólogos y equipos especiales que nunca antes habían estado en el territorio. Además, como es de conocimiento público, se está creando un Cesfam nuevo en Quintero y otro en Puchuncaví, y se va a construir un hospital nuevo de mayor categoría porque el que hay está en la cota de inundación, in embargo sostuvo que el esfuerzo más grande que pueden hacer por los 50.000 habitantes de Quintero Puchuncaví es asegurarles un futuro sin contaminación.

Hay expertos que dicen que este problema nunca se va a solucionar, así como hay gente que dice que no hay cambio climático, sin embargo señaló que se debe ser optimista y trabajar para solucionar el problema para que las más de 50.000 personas que viven en ese territorio puedan ver como recupera su belleza, su suelo, su agricultura, su turismo y su economía, aun cuando las empresas sigan trabajando sin dañar la salud de la población por la aplicación de un plan estricto que cumpla con criterios internacionales.

Sostuvo hay uno o dos casos de intoxicación diarios de forma alternada en los últimos veinte días y lo que establece una -y siguen con el tema de los principios precautorios- regla de causalidad bastante directa entre el control que han establecido a través de este sistema de alertas tempranas preventivas y la disminución de los episodios críticos. Estas alertas se activan cuando se presenta el fenómeno de inversión térmica, no hay viento, hay humedad y se presentan otras condiciones y mediante ellas se ordena disminuir significativamente las faenas de las empresas, incluso de aquellas actividades que no están normadas como las que generan elementos volátiles como los hidrocarburos COVs (Compuestos Orgánicos Volátiles). La disminución de las faenas sensibles, a lo menos en un análisis epidemiológico desde dos meses a la fecha actual, muestra una relación de causalidad con las situaciones críticas que piensa que es evidente, por lo que la medida de tener un sistema de gestión de episodios críticos, que además está incluido en el plan de descontaminación, parece ser exitosa. No obstante estas disminuciones el plan de descontaminación también establecen normas para sustancias que hoy no están normadas y un plan permanente de gestión de episodios críticos para el territorio, como el que se aplica hoy en Santiago donde nadie se alarma porque haya un plan de gestión de episodios críticos que cuando las condiciones ambientales puedan ser peligrosas para la salud permita tomar medidas drásticas para reducir las emisiones de todas las empresas, y sobre todo, aquellas que no tienen planes operativos, a las que se les reduce significativamente su operación.

Se trata de un tema país e indicó que el gobierno quiere un desarrollo sustentable y el desarrollo sustentable es aquel que es compatible con la vida y salud humanas, la integridad física y síquica de las personas y con el medio ambiente.

Respecto de los planes de emergencia y los sistemas de alarma que señaló el superintendente del Medio Ambiente, indicó que nunca la Superintendencia del Medio Ambiente por sí o por sus representantes sugirió establecer un sistema de

alarma. En todo caso opinó que mal lo podrían haber hecho porque en ese minuto no sabían la fuente directa que estaba causando la contaminación ni era el minuto para hacer operar una alarma. Si hubiese sido algo así de simple, así de fácil, por cierto que lo hubiesen hecho, tal como muchas otras medidas que tomaron en ese minuto y que probablemente ni siquiera son de conocimiento público, como asegurar el estado las alcantarillas en ambas comunas; asegurar la calidad del agua pública de pozo de Esval en las tres comunas, amén de otra serie de medidas que se adoptaron sin conocimiento público para asegurar de que no hubiese otros factores de riesgo que pudieran afectar a la población.

Contó que ha sostenido reuniones con los dirigentes de Enap y ellos han expresado su preocupación por la posible pérdida de empleo, y es algo que también han manifestado otros dirigentes gremiales de trabajadores con los que se ha reunido, y la explicación es la misma: el principio precautorio**.** Porque en los primeros días de la emergencia –esto es del 23, 24 y 25 de agosto, todos los elementos llevaron a la autoridad, que tiene por tarea investigar, fiscalizar y sancionar, que es la Superintendencia del Medio Ambiente así como a la Bridema, a fijarse en Enap por su cercanía. Pero esa es una función propia de la Superintendencia y no es nada personal en contra de Enap.

Acerca de las carencias o deficiencias del Sistema de Evaluación Ambiental, el Presidente Piñera también ha dicho que una de las tareas que queda es mejorar la legislación ambiental, que es laxa.

8.- SEÑOR JORGE BERMÚDEZ, CONTRALOR GENERAL DE LA REPÚBLICA.

Sobre el fallido plan de descontaminación de Quintero, explicó que cuando hablan de planes de prevención y descontaminación, se refiere a instrumentos de gestión ambiental que tienen como fin implementar medidas y acciones específicas tendientes a evitar la superación de normas de calidad ambiental en una zona latente o a recuperar los niveles señalados en estas o en una zona saturada por uno o más contaminantes.

Por lo tanto, el antecedente del cualquier plan de descontaminación es que exista una norma de calidad ambiental y que la autoridad ambiental haya declarado una zona latente o una zona saturada respecto de esos contaminantes.

Se debe tener presente que en Chile las normas primarias de calidad ambiental tienen alcance nacional, es decir, la norma de material particulado respirable, la del SO2 u otras tienen una vigencia para todo el territorio.

Así, puede ser que, se esté mirando las condiciones ambientales de la capital para regular una situación ambiental totalmente distinta a la que ocurre en la capital, que es una cuenca, que está cerrada, que tiene otras condiciones de ventilación y otros contaminantes. Por lo tanto, el hecho de que se esté cumpliendo con la norma ambiental, no quiere decir que no haya contaminación, y ese es un dato clave en este caso.

El punto es que no existen normas secundarias, que serían las territoriales en esta materia y, por lo tanto, rigen las normas que son generales para todo el territorio nacional. Y si bien eso está establecido opinó que era un error, atendida la diversidad ambiental, geográfica y territorial de Chile.

Ahora, para dictar un plan de descontaminación hay un proceso que es largo, muy extenso y reglado, a diferencia de otros procedimientos normativos en que se dictan reglamentos. Existen una serie de pasos como: La elaboración del anteproyecto de plan, que implica un desarrollo previo de estudios; la conformación de ciertos comités y subcomités operativos, y el denominado Agies, que es el análisis general del impacto económico y social. Se contempla un plazo para consulta pública, que es lo que ocurre con el plan que se encuentra en tramitación en este momento, en el que se lleva a cabo un análisis de las observaciones que son formuladas. Se elabora el proyecto definitivo del plan, el que pasa para su d) aprobación al Consejo de Ministros para la Sustentabilidad, y enseguida es remitido al Presidente de la República para que elabore el DS, el que pasa después a la toma de razón de la Contraloría.

A diferencia de lo que ocurre en otros sectores, economía o minería o en cualquier otro, la relación del Ministro con el Presidente es directa, en materia ambiental las decisiones relevantes pasan primero por el Consejo, el cual tiene una visión de complementar esa mirada y darle una visión más transversal y multidisciplinaria y obviamente ocurren cambios en esa normativa propuesta cuando pasa por el Consejo de Ministros para la Sustentabilidad.

Sobre el plan para las comunas de Concón, Quintero y Puchuncaví representado por la Contraloría, sostuvo que se debe tener presente que en este instrumento se debe buscar que las normas primarias se cumplan, es decir, que se pueda volver a una situación de normalidad.

Así el plan tenía por objetivos: primero evitar la superación de la norma primaria de calidad ambiental para MP10 como concentración anual y, en segundo lugar, evitar la superación de la norma primaria de calidad ambiental para material particulado fino, es decir, la partícula más pequeña que es MP2,5, como concentración de 24 horas, y luego, recuperar los niveles señalados en la última norma mencionada de material fino como concentración anual que es de 20 microgramos por metro cúbico normal de aire. Todo ello en un plazo de seis años, a pesar de que había -y eso hay que aclararlo- una disparidad que se produjo en su momento en la tramitación respecto de los plazos.

Explicó que la tramitación fue muy extensa, hubo varias entradas y salidas de la Contraloría, para evitar la representación directa que se podría haber hecho el día 15. Es decir, para evitar que todo este proceso tan complejo, tan extenso y tan reglado se hubiese caído producto de observaciones que se podrían haber salvado con una conversación o con una mesa de trabajo, que fue lo que efectivamente ocurrió a lo largo de esta tramitación.

Comentó que la Contraloría planteó 109 observaciones y no solo formales por problemas de referencia, sino también cuestiones técnicas y de legalidad, y dudas que debían aclararse. Así llegó el mes de diciembre con cuatro observaciones dos se subsanaron y las otras dos no fueron solucionadas por el Ministerio y hubo que representar el plan.

Las observaciones subsanadas son:

La disparidad desde el punto de vista del plazo de seis años, que estaba prevista en el anteproyecto y que después se aumentaba sin ninguna razón ni fundamento a diez; el concepto de caldera existente, elemento muy importante, porque las calderas son una de las fuentes emisoras de contaminantes atmosféricos.

El concepto de caldera existente apareció durante la tramitación ante la Contraloría. O sea, este concepto era distinto en la tramitación del plan, que luego, sin ningún antecedente, se cambia y se señala que caldera existente es aquella que está registrada por la autoridad sanitaria con posterioridad a un año calendario desde que fue publicado el plan, lo que no tenía ningún sustento técnico ni había algún antecedente durante la tramitación.

Señaló que es un concepto bien importante, porque en el fondo es una especie de ficción, ya que por caldera existente uno diría que es lo que hoy existe; sin embargo acá, caldera existente es la que existe hace más un año más. Es decir, todas las que además se inscriban en el proceso un año después. Es un tratamiento mucho más beneficioso, porque la caldera existente tiene una norma mucho más laxa que la caldera nueva.

Hubo dos grupos de observaciones que no fueron subsanadas.

1.- Los niveles de emisión consignados en el inventario de emisiones respecto de las fuentes puntuales, las tres principales: Codelco, Enap y Aes Gener son superiores a los que constan en el informe técnico contenido en el expediente, habiendo sido modificado mediante una estimación efectuada por el Ministerio del Medio Ambiente, suponiendo el escenario con mayor impacto ambiental.

¿Qué quiere decir esto? Que durante el proceso de elaboración del plan se trabajó con las emisiones reales. Es decir, lo que efectivamente emitían las empresas, lo que, obviamente, da cuenta de su operación y de los esfuerzos que habían hecho históricamente las empresas para disminuir sus emisiones. Sin embargo, en el plan se consideró el peor escenario posible, es decir, las fuentes funcionando los 365 días al año, 24 horas al día, sin considerar, por ejemplo, que tienen que paralizar para hacer mantención o que hay períodos de baja, cuando se trata de una generadora eléctrica, por ejemplo.

Entonces, ¿qué ocurre? Se fijaron niveles de contaminación muy altos y muy por sobre de lo que se había efectivamente contaminado en un determinado periodo. Por lo tanto, si tomo ese techo tan alto, sin hacer nada, estoy cumpliendo, no tengo que hacer ninguna reducción adicional.

Consideró que esta fue una observación muy relevante a propósito del análisis de este plan. Indicó que tuvo conversaciones informales en el Ministerio y personalmente le explicó al Ministro de la época las razones para representar el plan, más allá de lo que quedó plasmado en el oficio. Luego, vino febrero y se acabó el año hábil, desde el punto de vista de la gestión del gobierno.

INVENTARIO DE EMISIONES DEL AGIES[41]

EMISOR	**Emisión (ton/años)**				
	MP	**MP_{10}**	**MP_5**	**NO_X**	**SO_2**
AES GENER	382	351	288	8.557	10.301
CODELCO	325	286	202	0	13.743
ENAP	1.170	732	425	1.197	1.711

[41] Inventario de misiones utilizado en evaluación económica año 2013.

Lo que pueden observar en la tabla es lo que aparece como inventario de emisiones en el análisis general del impacto económico social, es decir, lo que está basado en el informe técnico, tomando como base el año 2013. Por ejemplo, para material particulado fino, para el óxido nitroso y dióxido de azufre, etcétera. Las distintas cantidades de toneladas que emitían los generadores.

Si se compara con lo que efectivamente quedaba en el plan, por ejemplo, para Aes Gener, en material particulado, según el informe técnico, emitía 382 toneladas; sin embargo, en esa ficción, en ese modelo que se utiliza, se dice que Aes Gener funcionando 365 días, 24 horas al día, va a emitir 1.033, pero en realidad no emite 1.033, sino que 382. Así lo mismo para Codelco, en donde la diferencia no es tan grande, y respecto de Enap que incluso la diferencia podría haber sido beneficiosa.

Para los precursores de material particulado es un poco peor la situación por el dióxido de azufre. Por ejemplo, en Aes Gener hay una diferencia de más de 5.000 toneladas; en Codelco, mil y fracción, y en Enap, 300 y fracción de toneladas.

NIVELES DE EMISION SEGÚN INVENTARIO AGIES v/s
Niveles de Emisión Plan

Contaminantes (Toneladas/ años) Fuente	MP AGIES	MP Anteproyecto y Plan
AES GENER	382	1033
CODELCO	325	390
ENAP	1.170	1.103

Contaminantes (Toneladas/ años) Fuente	SO2 AGIES	SO2 Anteproyecto y Plan
AES GENER	10301	15275
CODELCO	13743	14799
ENAP	1711	2148

Contaminantes (Toneladas/ años) Fuente	NOX AGIES	NOX Anteproyecto y Plan
AES GENER	8.557	10317
CODELCO	n/a	n/a
ENAP	1197	1475

Ante el comentario de que Aes Gener es la más beneficiada o la que tiene la mayor diferencia, respondió que así era porque su techo era más alto, pero su emisión real era la más baja. Entonces, no tendría que hacer ningún esfuerzo, porque con la sola entrada en vigencia del plan ya lo estaba cumpliendo.

En resumen, respecto de este grupo de observaciones, ellos dijeron que el inventario que se utilizaba para el plan suponía el escenario con mayor impacto ambiental. Es decir, máximas emisiones autorizadas y a máximas capacidades operacionales de las plantas, 365 días por año, a 24 horas.

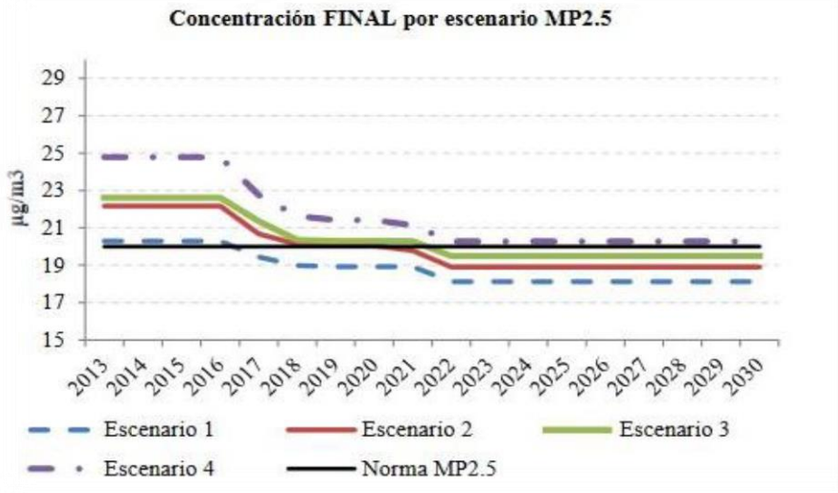


Figura A: Reducción concentración anual $MP_{2,5}$.

La reducción de la concentración anual para $MP_{2,5}$ alcanza el objetivo propuesto por la norma de 20 µg/m^3 para los escenarios 1 en el año 2017, escenario 2 el año 2021 y escenarios 3 y 4 el año 2022. El escenario 4 constituye el escenario más desfavorable donde la concentración se aproxima a los límites de la norma.

En relación a este gráfico explicó que esta figura se utiliza también en el plan. Los colores no se distinguen muy bien, pero el escenario cuatro, que es este escenario hipotético, en el año 2022 es el más desfavorable donde la concentración se aproxima a los límites de la norma. En la línea punteada y segmentada que está más arriba, en realidad, la línea real es solo la segmentada. O sea, si se puede ver en la presentación esa sería la real y las disminuciones que se deben hacer.

Como el modelo toma como año base el 2013 y las emisiones son las que allí aparecen, los años de disminución son a partir de 2017, cuando se suponía que el plan entraba en vigencia. En 2018 debía hacer esas reducciones, y la línea negra que aparece entre los números 19 y 21, es lo que establece la norma. Por lo tanto, para llegar a esta situación de cumplimiento normativo, las empresas tenían hasta el 2023-2024 pero en realidad estaban cumpliendo desde siempre o casi desde siempre, pues era muy poco lo que tenían que disminuir en general.

Afirmó que lo explicado tenía incidencia en la configuración de las medidas de reducción de emisiones, las distintas tablas van dando cuenta de esas reducciones. Por ejemplo, el límite máximo que aparece para Codelco División Ventanas de SO2, para el primer año de entrada en vigencia son 14.650 toneladas, pero según el informe técnico que tenían, o que en realidad estaba como antecedente del plan, lo que emitía como base Codelco eran 13.743 toneladas. Por lo tanto, Codelco entraba cumpliendo ese plan originalmente, o sea, no tenía que hacer nada distinto de lo que ya estaba haciendo, y así sucesivamente. Lo otro es un poco repetir el mismo esquema respecto de cada uno de los contaminantes en que básicamente se cumplía de entrada.

Ante diversas consultas, contestó que a propósito del análisis del plan que ingresó a la Contraloría dijeron que el plan tiene un objetivo, cual es lograr el cumplimiento normativo y, por lo tanto, en este caso descontaminar. Si entra en vigencia el plan, la empresa, sea cual sea, el emisor que sea, no tiene que hacer nada y no supone una reducción de sus emisiones, en realidad no está logrando el objetivo legal que tiene el plan, cual es que descontamine, que aunque parezca una paradoja lo que estaba haciendo simplemente era ajustando las emisiones que hoy tenía al cumplimiento normativo.

Manifestó no entender por qué se utilizó esa metodología, cuyos números no coincidía, primero, con el objetivo del plan y, segundo, con los propios antecedentes del propio plan, porque se basaba en un antecedente técnico distinto.

Ahora, también es cierto que las emisiones totales que hoy existen de estas empresas ponen la situación levemente por sobre la norma primaria. Es decir que tal vez con poco esfuerzo las empresas pueden lograr no solo cumplir con la norma, sino que salir de una situación de declaración de zona saturada y pasar a la zona más beneficiosa, que sería de latente, pero ya no es un plan de descontaminación, sino de prevención.

Enfatizó que el problema se debía a la laxitud de las normas porque se habla de normas de alcance nacional que se dictan pensando en Santiago y no pensando en cuál es la realidad del territorio.

Afirmó que sin ser pesimista, un instrumento que se fija solo en la norma primaria probablemente no va a dar todos los resultados que podría tener si tuviera un enfoque un poco más completo, que no existe en nuestra legislación. Ese enfoque no existe.

Sobre las RCA de los grandes generadores, indicó que normalmente sí tienen resolución de calificación ambiental, ya que son las plantas más antiguas, o parte de instalaciones antiguas, las que no tienen resolución de calificación ambiental.

Agregó que no obstante la RCA el parque sigue creciendo porque estos instrumentos normalmente tienen un tope de emisiones. Entonces, las empresas han ido haciendo reducciones de esas emisiones y, por lo tanto, están dentro del cumplimiento normativo.

Sin embargo hay que tener presente que cuando una empresa tiene un delta de emisiones porque mejoró el proceso o porque alguien hizo una inversión que hizo mejorar el proceso, lo vende, y eso que es bastante informal ha contribuido a que no mejore la condición ambiental, porque esa liberación de emisiones hace que otro venga y pueda ocupar ese espacio para poder instalarse en ese territorio.

Respecto a la segunda observación, indicó que se debió a que los límites de máximos de emisión para las calderas, eran superiores a lo establecido en el anteproyecto, sobre todo respecto de los precursores del material particulado.

Esto tiene bastante importancia, porque en el anteproyecto y en todo lo que se venía discutiendo, se habían fijado valores para las calderas. Por ejemplo, una caldera existente podía emitir 50 microgramos por metro cúbico normal de SO2. Sin embargo, lo que se aprueba es cuatro veces más alto, lo que es un número mágico; o sea, ese número simplemente aparece. Como Contraloría, no pueden decir si 50 o 200 es lo deseable, pero sí pueden decir que parece raro que el número 200 aparezca simplemente y no tenga un antecedente en el anteproyecto.

Por lo tanto, la Contraloría concluyó que ese instrumento de gestión ambiental no cumplía con la finalidad que la normativa le asigna, cual es descontaminar.

Consultado sobre dónde se produjo el cambió en el inventario, sostuvo que le da la impresión que fue previo a que ingresara al Consejo de Ministros.

Sobre el decreto N° 83, del 25 de septiembre de 2018, de alerta sanitaria, que otorga algunas facultades para la Seremi de Salud, que, básicamente, se traducen en la posibilidad de que la autoridad sanitaria pueda ordenar la disminución o la prohibición de funcionamiento de instalaciones, según lo aconsejen las circunstancias sanitarias, indicó que su vigencia era hasta el 30 de marzo de 2019.

Acerca de si se puede paralizar o no las faenas, precisó que el decreto está consignado en términos bastante amplios; o sea, es reducir o prohibir. La prohibición no dice si puede ser total o parcial, por lo tanto, teóricamente se puede disponer un cierre completo de la actividad, pero se está hablando de instalaciones que son muy complejas. Por ejemplo una refinería no tiene un *on-off*; o sea, que se pueda encender y apagar. Es decir, cuando se produce el proceso de bajada de una refinería, de cobre o de petróleo, que a veces se ha producido abruptamente, por terremoto se produce más contaminación que si estuviera funcionando. Entonces debe ser programado el proceso de bajada de esas instalaciones tan grandes.

Por lo tanto, si la pregunta es estrictamente jurídica, obviamente la respuesta es afirmativa por lo que podría paralizarse en teoría, pero la decisión es más, porque técnicamente, incluso ambientalmente, puede tener muchas consecuencias.

Ante la pregunta de si se hubieran podido evitar estos episodios de emergencia si hubiera estado vigente el plan de descontaminación, señaló que es difícil saberlo, porque todavía no está muy claro cuál fue la fuente emisora a la que se le debe atribuir estos eventos o si fueron todas juntas, o en realidad se trató de una situación totalmente distinta de lo que se está analizando.

Por lo tanto, faltan normas de carácter horario, que permitirá medir cada una hora lo que actualmente se mide cada 24, con niveles de exigencia más altos, ya que la falta de ella hace que para advertir contaminación se promedian 24 horas o se calcula el promedio del año, lo que resulta muy amplio, porque fácilmente en una semana puedo netear un día con otro y, más todavía en un año. Añadió que no sólo faltan normas de arsénico y de calidad de suelo.

9.- SEÑORA MARÍA ARAYA, PRESIDENTA DEL CONSEJO CONSULTIVO DE SALUD DE QUINTERO.

Expresó que si bien la situación de emergencia se verificó el 22 de agosto, el Consejo Consultivo de Salud de Quintero había alertado 2 o 3 meses antes al Ministro, intendente y Seremi de Salud la situación de peligro que se aproximaba, informándoles de las posibles consecuencias ambientales e indicándoles el riesgo que significaría una nube tóxica en la comunidad de Quintero y que el hospital no estaba en condiciones de mitigar las consecuencias de una emergencia medioambiental.

Agregó que una vez que se presentó la emergencia, recién se evidenció una reacción del gobierno, brindando medidas de mitigación, ofreciendo un hospital de campaña y especialistas. Sin embargo, ello solo se concretó de lunes a viernes de 8 a 17 horas.

Manifestó una problemática considerable, en relación al número de médicos y el alto número de personas intoxicadas, así la noche del 9 de septiembre

en el área de emergencias solo habían disponibles dos médicos, dos enfermeras y dos técnicos en enfermería, quienes se encontraban atendiendo pacientes por intoxicación, provenientes de Quintero, Puchuncaví y Loncura. Esto evidencia el colapso que presenta el hospital, y que se traduce en 6 especialistas de la salud para más de 60 personas que se encontraban a las afueras de la unidad de emergencia.

Indicó que el 8 de septiembre se produjeron 13 episodios de contaminación, sin embargo, se les solicitó guardar calma pues irían disminuyendo con el transcurso de los días, pero al contrario fueron aumentando.

Señaló que no se ha considerado a la emergencia sanitaria como un factor relevante ya que ésta a diferencia de la emergencia ambiental faculta al Ministerio de Salud a tomar decisiones enérgicas, como cerrar instalaciones y empresas de forma inmediata por peligro sanitario.

Agregó que el gobierno tiene conocimiento de esta situación y también que en el hospital de Quintero se atienden alrededor de 60.000 pacientes entre niños y adultos. Pese a esta cifra y a la alerta amarilla medioambiental y sanitaria el hospital de campaña atiende de lunes a viernes, de 8 a 17 horas.

Opinó que es imprescindible cambiar la normativa actual relativa a gases, en el sentido de ampliarla a los metales pesados, pero por sobre todo saber cuáles son las empresas que contaminan.

10.- SEÑOR ALEXIS ROJAS, DIRIGENTE ESTUDIANTIL COMUNA DE QUINTERO.

Indicó que la primera nube tóxica se produjo el 22 de agosto y provocó la evacuación de los alumnos de sus aulas de clases, debiendo ser trasladados a sus hogares, sin embargo, dada las complicaciones de salud que se presentaron la gran mayoría fue derivado a los hospitales y se suspendieron las clases. Frente a ello las autoridades aseguraron que la situación era extraordinaria y que se encontraba bajo control, por lo cual el jueves 23 de agosto se retomarían las actividades académicas. Así día siguiente se reanudaron las clases, no obstante, al medio día nuevamente los colegios de Quintero y Puchuncaví debieron ser evacuados, evidenciándose más de 200 intoxicaciones y las clases se suspendieron dos semanas.

Señaló que el 7 de septiembre se levantó la alerta amarilla decretada, el lunes 8 se realizó la jornada de reflexión para los profesores, y el martes 9 los alumnos regresaron a clases, sin embargo, antes de las 2 de la tarde nuevamente se produjeron episodios de intoxicación, debiendo reiterar las medidas de evacuación junto con la suspensión de clases.

Por esto los alumnos acordaron realizar una toma simbólica del establecimiento en forma de protesta, antes de que ocurriera el *peak* de contaminación y de la nube de tóxica. Por ello los estudiantes del colegio Santa Filomena hicieron ocupación del establecimiento como una forma de ejercer presión y llamar la atención de la prensa.

Informó que son siete los establecimientos que se encuentran en ocupación por sus estudiantes, y aun cuando saben que se trata de una toma simbólica, es una manera de captar la atención de las autoridades.

Sostuvo que si bien cada establecimiento educacional tiene sus propias exigencias, existe un punto en común, y este es exigir garantías verdaderas de que no existirá un nuevo episodio de contaminación en los colegios. Para ello solicitó la paralización del parque industrial hasta que se sepa con certeza cual empresa contamina -ello si se puede porque no hay una unidad de monitoreo móvil que pueda determinar de dónde emanan los contaminantes-; la dictación de nuevas normas de calidad ambiental atmosférica y la homologación de las existentes, de acuerdo a las guías propuestas por la Organización Mundial de la Salud.

11.- SEÑOR HERNÁN RAMÍREZ, INVESTIGADOR ASOCIADO A LA FUNDACIÓN TERRAM.

Indicó que la Comisión Especial Investigadora de la Cámara de Diputado que se constituyó el año 2011 para investigar este tema determinó que el Estado tenía responsabilidad en la contaminación histórica de esta zona e hizo 24 recomendaciones al Estado de las cuales se dio cumplimiento sólo al 17%.

Se refirió al avance de las principales recomendaciones de esta Comisión, las que en la figura se destacan en amarillo.

N° en informe	**Propuesta**	**Avance**	**Antecedentes**
1	Estudios que conduzcan a la remediación de suelos aledaños a las zonas afectadas.	60%	MMA encarga estudio año 2015 que miden presencia de metales pesados, As, Cu, Cd, Pb entre otros. Se han realizado algunos experimentos relacionados a la biorremediación de suelos pero ninguna medida concreta. Ultimo estudio indica que faltan nuevos estudios de biodisponibilidad.
2	Glosa especial de presupuesto para mitigar efectos del daño medioambiental.	0%	No existe glosa de presupuesto del MMA ni de gobierno Regional destinado a la mitigación ambiental.
3	Exigir inversión en tecnología de punta para empresas del parque industrial, a partir del año 2012	0%	No se conoce que el Estado exigiera la implementación de esta tecnología (termoeléctricas unidades I y II siguen vertiendo aguas caliente en la playa de Ventanas, Fundición Cobre no ha cambiado tecnología horno Flash. No existe sustento jurídico para que la autoridad exija inversión en tecnología de punta solo existe exigencia de cumplir la norma).
4	Estudio de línea base de contaminación de metales pesados en la zona	60%	3 de los cuatros estudios de riesgo encargados por el MMA (2011) confirmaron presencia de metales pesados en suelo, aire y recursos marinos. No se han tomado medida ni realizados estudios en hogares de Quintero y Puchuncaví, ni nuevos estudios en escuelas
5	Estaciones de monitoreo pasen a ser administradas por el MMA	0%	Nada siendo mantenidas y calibradas por técnicos contratados por las empresas, quienes remiten dicha información al Ministerio.
	Red de monitoreo digital y en línea, disponible para el público.	50%	Ya existía en el 2011 la Red Ventanas en línea. La estación de Monitoreo del Puerto Ventanas en Campiche así como la estación de Loncura no han ingresado al sistema en línea.

	Exigir aumento de estaciones y mejora de tecnología.	50%	Según MMA las estaciones cumplen normativa no se ha solicitado mejora. Estación de Puerto Ventanas que tiene en Campiche no funciona o tiene problemas. No se han incrementado las estaciones de monitoreo. La última estación de monitoreo que entro a funcionar fue Ventanas en 2013 que fue comprometida en la RCA de la termoeléctrica a Carbón Campiche del año 2008.
6	Reformulación del plan de descontaminación de 1992 y considere a todas las empresas del complejo y haga mediciones de MP 10, MP 2,5 y SO2.	20%	La reformulación o "actualización del plan de descontaminación de 1992" se transformó en el nuevo Plan de Descontaminación. El expediente fue abierto bajo el nombre de actualización pero con la entrada en vigencia de la norma calidad MP2.5 la zona fue declara saturada (DS10 /2015) y cambia el nombre a Plan de descontaminación y Prevención comunas Concón, Quintero y Puchuncaví, rechazado por Contraloría.
	El nuevo plan de descontaminación debe contar con actualizaciones de las normas medioambientales, incluyendo mediciones de SO2, MP 10 y MP 2,5.	0%	La norma de MP 2.5 entro en vigencia el mayo 2011, las normas de SO2 y Mp10. no han mejorado sus parámetros en estos años en comparación a lo recomendado por la OMS
7	Revisar y ajustar plan de operación ante episodios críticos.	0%	No existen restricciones legales para el funcionamiento de empresas frente a situaciones de mala ventilación atmosférica. Tampoco lo incluía el plan de descontaminación rechazado por Contraloría.
	Incorporar normas horarias como norma primaria	0%	Esto se refiere a la norma de SO2. Todavía no se modifica de manera de incluir normas horarias.
8	Establecer sistema de alarma preventivo de contingencia financiado entre privados y el Estado.	0%	No existe.
	Fondo de salud para las personas afectadas en la zona por la actividad	0%	No existe.
	Recuperar ecosistemas con fondo permanente entre empresas y Estado	0%	No existe.
9	Solicitar al Ejecutivo evaluar la implementación de impuestos al carbono u otros impuestos verdes.	100%	El llamado impuesto verde fue aprobado el 2015 como norma nacional, pero su impacto ha sido criticado ya que muchas empresas rebajaron este impuesto.
10	Estudiar proyecto de ley que considere efectos sinérgicos y acumulativos de proyectos ingresados al SEIA.	0%	No existe.
11	Instar al Ejecutivo que modifique la regulación sobre calificación industrial contenida en el art 4.14.2 Ordenanza Urbanismo y Construcción.	0%	?
12	Dictar norma para fundiciones que regule emisiones de contaminantes peligrosos.	100%	DS 28/2013, sin embargo la norma es básica en lo que requiere o en la exigencia de capturar contaminantes; 95 por ciento, no obstante la

			tendencia internacional es 98 por ciento para la captación de gases.
	Norma para caracterizar contaminantes en carbón utilizado como combustible.	0%	No existe
	Norma de calidad de metales pesados en aguas y fondos marinos	0%	No existe
13	Plan de compensación para trabajadores con salud afectada por exposición a contaminantes en faena.	0%	Nada nuevo a este respecto. Solo lo que establece la ley 16744 respecto a salud laboral
	Compensación para familiares de quienes perdieron la vida por las condiciones ambientales de la faena.	0%	Se refiere a los ex trabajadores de ENAMI y sus familiares
14	Exámenes médicos periódicos y obligatorios para trabajadores.	0%	Habría que consultarlo a las mutuales de trabajadores
	Proseguir con exámenes médicos para habitantes de la zona, periódicos y aleatorios	0%	No existe
15	Instauración de protocolos de avisos obligatorios, públicos y coordinados por las empresas para trabajadores, comunidad y autoridades en episodios de emergencias en tiempo real.	0%	No existe
16	Identificación y señalización de lugares donde la contaminación representa un riesgo para la salud.	0%	No existe
17	Incorporar a las comunidades en el APL entre CPL y empresas de la zona.	50%	Preguntarle a ASIVA que se avanzo
18	No permitir la modificación del carácter de zona saturada hasta que se dicte plan de descontaminación.	100%	Se ha mantenido la declaración de zona saturada a pesar que el plan de descontaminación no ha sido aprobado
19	Solicitar al Presidente la modificación de la norma primaria de SO2	0%	Todavía no se modifica.
20	Elaborar normas primarias de calidad de suelo y agua	0%	No existe
21	Establecer planes de descontaminación para suelo y agua.	0%	No existe
22	Se insta a las Seremias a no utilizar sus facultades en el cambio de uso de suelo rural mientras no se regule la existencia de instrumentos de planificación.		
23	Se sugiere a la autoridad marítima no otorgue más concesiones marítimas mientras no se cuente con un plan de ordenamiento del borde costero.	0%	Se han entregado nuevas concesiones marítimas a pesar de no existir plan de ordenamiento borde costero.

	Modificación de normativa para otorgamiento de concesiones, incluyendo consideraciones medioambientales.	0%	No existe
24	Las empresas deberían generar inversión para la confección de un plan de recuperación y desarrollo sustentable de la biodiversidad y calidad de vida de las personas.	0%	No existe
		17%	

Relató además, que a partir del año 2011 se generaron estudios de metales pesados en los diferentes colegios; en la comuna de Puchuncaví. Así en 14 establecimientos se analizó el polvo al interior de la sala y de suelo en los patios u el resultado fue que todas las dependencias registraban la presencia de metales pesados; razón por la que el ex Seremi de Salud Jaime Jamett ofició estos resultados al Subsecretario de Educación de la época, indicándole la imperiosa necesidad de establecer un plan regulador permanente de limpieza industrial y de vigilancia epidemiológica en la totalidad de los establecimientos evaluados. Pese a ello hasta la fecha no se ha realizado ninguna de estas acciones.

Continuó su exposición refiriéndose a un estudio del año 2015 respecto a niveles de arsénico y advirtió que todas las estaciones: estación Sur, Valle Alegre, La Greda, Maitenes y Puchuncaví superan ampliamente el máximo de arsénico recomendado por la OMS. Todas las estaciones presentan niveles sobre la norma. En el caso de La Greda, 23 veces sobre la norma, en 2015.

Comentó que no hay una norma de calidad primaria de arsénico, a pesar de que las mediciones de arsénico en Puchuncaví y Quintero superan en varias veces el máximo recomendado por la OMS de 6 Ng/m3N. Si existen normas de emisión, normas que permiten tirar arsénico hacia la atmósfera. En el caso de la fundición de cobre, permite, anualmente, 48 toneladas de arsénico, que las cumple.

Sobre la presencia de metales pesados en los recursos marinos en las localidades de Ventana, Zapallar, Cachagua, Maitencillo, Horcón, Ventana, Quintero, indicó que Oceana, en el año 2012, realizó un estudio que confirma la presencia de metales pesados en locos, lapas y jaibas del área de manejo del Sindicato de Pescadores de Ventanas. En 2014, son vertidos por la ENAP, 38.000 litros de hidrocarburo en la bahía.

Desde 1992 han ocurrido 10 derrames a la bahía, de diferentes componentes. En 1992, de percloroetileno, de Oxiquim. Posteriormente, en 2008, 180 toneladas de 2-etilhexanol al Puerto Ventanas. Este año hubo dos episodios de derrame de petróleo en la bahía.

Un estudio en el año 2015 determinó que 57 por ciento de los locos sacados en la zona de Cachagua supera normas de cadmio y cobre. En el caso de la jaiba, el 86 por ciento; la lapa, el 56 por ciento, y el erizo, el 75 por ciento. En Maitencillo el 100 por ciento de las jaibas y el 67% de los locos excedieron normas de cadmio y cobre. En Horcón, el 92 por ciento de las jaibas supera la norma y el 50 por ciento de los erizos.

Para el caso de Ventanas se realizan un total de 32 muestreos, de los cuales el 43,8% supero normas cadmio y cobre principalmente. El 100% de las jaibas y el 44% de lapas superaron normas para cobre y cadmio. Cabe señalar que el 100%

de los erizos analizados cumple norma sanitaria, de acuerdo a los compuestos analizados.

Dentro de la bahía de Quintero, el 50 por ciento del loco y casi el 100 por ciento de las jaibas superan la norma, frente a ello lo que preocupa es que la gente se come estos productos.

Respecto a las Normas de Calidad Primaria del Aire, señaló que la norma de Material Particulado Respirable MP10 no ha tenido mejoras en sus estándares desde 1998. En 2014 se inició su proceso de revisión, sin embargo, no se contemplaron mejoras a sus estándares, los que sobrepasan al máximo recomendado por la OMS y al máximo permitido en Estados Unidos y la Unión Europea. Es necesario señalar que el Material Particulado es el contaminante que más significativamente ha sido asociado a eventos de mortalidad y morbilidad en la población.

La situación es igual al analizar comparativamente las NCP para Material Particulado Fino Respirable MP 2.5, Dióxido de Azufre (SO2) y Dióxido de Nitrógeno (NO2). En Chile no hay Normas de Calidad Primaria para el arsénico (As), Benceno, Tolueno, Xileno, Mercurio, Cadmio, Vanadio y Compuestos Orgánicos Volátiles (COV).

Culminó su presentación planteando las estrategias propuestas al Ministro de Salud durante julio, las que corresponden: a red de monitoreo no dependiente, implementación de planes de contingencia en episodios críticos, cumplimiento del dictamen de Contraloría respecto de la limpieza de escuelas, modificación urgente de materias energética de la zona, implementación de normas sobre calidad de arsénico en el aire, implementar urgente una norma primaria para suelo, homologación de todas las normas ambientales con las de la OMS.

12.- SEÑORA KATTA ALONSO, EN REPRESENTACIÓN DEL MOVIMIENTO MUJERES DE ZONA DE SACRIFICIO QUINTERO EN RESISTENCIA.

Relató que el 8 de junio, 25 niños del complejo educacional Sargento Aldea fueron atendidos tras sufrir intoxicaciones. Recordó que estos hechos se habían repetido con anterioridad, el 23 de marzo de 2011, en la escuela La Greda, se registraron 23 menores y 7 adultos intoxicados; el 31 de agosto del mismo año en la escuela Alonso de Quintero, 24 alumnos y 1 profesora intoxicados; el 24 de noviembre de 2011, en la escuela La Greda, 31 alumnos y 11 adultos intoxicados; el 14 de septiembre de 2015, en la Nueva Escuela de La Greda, 20 alumnos aparentemente intoxicados por la emanación de fuertes olores; el 23 de marzo de 2017, en el complejo educacional Sargento Aldea, de Ventanas 19 alumnos intoxicados; el 5 de abril de 2017, el mismo colegio en Ventanas; el 14 de marzo de 2018, en la Escuela de Chocota, y el 20 de mayo del año 2018, durante el desfile se produjeron intoxicaciones.

Advirtió que durante el mes de agosto, fueron trasladas por intoxicación, a los recintos asistenciales 508 personas; en septiembre, 826; y hasta el 4 de octubre, 81, registrando aproximadamente a la fecha 1.415 personas.

Indicó que las medidas adoptadas por el Ejecutivo han sido insuficientes, razón por la que solicitan como movimiento detener el funcionamiento del parque

industrial hasta lograr que se determinen las causas de las intoxicaciones sufridas por la comunidad.

Sostuvo que los parlamentarios presentes en la localidad de Puchuncaví, tomaron conocimiento de la situación ocurrida en Codelco, y a través del relato de uno de sus trabajadores, se evidenció que la empresa sigue funcionando exactamente igual desde antes del plan de emergencia como en la actualidad, al igual como ocurre con AES Gener, que en las noches tiene funcionamiento con normalidad.

Agregó que el informe que mandó a elaborar ASIVA a una empresa externa concluyó que había presencia del mercaptano, -hidrocarburo volátil- y los síntomas que provoca son -adormecimiento de las extremidades inferiores y superiores-, junto con metilcloroformo arrojado por Oxiquim y que las empresas no cumplían la norma porque siguen registrándose peak de CO2, además, en las noches AES Gener continua emitiendo CO2 superando lo permitido.

Advirtió que en la primera fiscalización efectuada a la empresa Gasmar, se detectó una fuga de gas con mercaptano**,** sin embargo, esto no fue informado.

Indicó que 60% de las empresas del barrio industrial funcionan sin Resolución de Calificación Ambiental y 80% sin resolución sanitaria y que cuando los fiscalizadores fueron a inspeccionar Codelco Ventanas tuvieron que usar mascarilla porque no soportaban la contaminación.

Respecto de Puerto Ventanas, manifestó no entender cómo seguía funcionando con los continuos varamientos de carbón en la playa Ventanas.

Sostuvo que playa ventanas era muy concurrida especialmente la cercana a los muelles de AES Gener, en donde el agua es caliente, no obstante es necesario cerrarla porque está muy contaminada por los metales.

Enfatizó la necesidad de homologar las normas de calidad del aire a las que tiene de la OMS, la creación de normas para hidrocarburos volátiles, metales pesados y para suelos, aguas y aguas saladas. Asimismo indicó que toda la población quiere el cierre de la fundición de Codelco, porque es la que más contamina; junto con las termoeléctricas de AES Gener, partiendo de forma inmediata por la uno y la dos, además del congelamiento del parque industrial, independientemente de las 569 hectáreas.

Expuso que de acuerdo a las cifras registradas en el Plan de Contaminación impugnado por del movimiento Mujeres de Zona de Sacrificio Quintero en Resistencia y rechazadas por la Contraloría General de la República, se advirtió la imposibilidad de continuar con el funcionamiento de las empresas tras la superación excesiva de los márgenes de contaminación.

Llamó al gobierno al diálogo con la sociedad civil y los expertos de ambas partes -comunidad y gobierno- con el objeto de determinar soluciones a las situaciones ocurridas en las diferentes localidades.

13.- SEÑORA DANIELA MUÑOZ, FUNCIONARIA DEL HOSPITAL DE QUINTERO Y DIRIGENTE DE LA ASOCIACIÓN DE PROFESIONALES DEL SERVICIO DE SALUD.

Explicó que su exposición estaba centrada en la opinión de los socios de la multigremial de Quintero, comprendida por los gremios existentes en el hospital, FENATS Unitaria y FENATS Nacional.

Sostuvo que los habitantes de las comunas afectadas por la contaminación de las empresas de la zona están cansado de soportar desde hace más de 50 años tener que respirar los contaminantes emitidos por ellas.

Indicó que tras los episodios de emergencia sufridos, los funcionarios del hospital se encuentran en un estado de constante stress, ya que deben dar información sobre las posibles causas de los síntomas de la intoxicación, sin que cuenten con estudios concretos o pruebas que permitan avalar lo que le dicen a la población. Agregó que las medidas instauradas por el gobierno no solucionan la raíz el problema de la contaminación, sino más bien, atacan los síntomas.

Evidenció la falta de recursos para la atención de salud en relación a los continuos episodios de intoxicación que sufre la población y a la cantidad de personas que viven en las comunas afectadas. De contar con ellos, sostuvo, se podría otorgar una cobertura como corresponde, y realizar acciones preventivas, curativas y rehabilitadoras para los pacientes.

Manifestó que los funcionarios de la salud que trabajan en las comunas afectadas, producto los episodios de intoxicación sufridos por la población, han experimentado estrés constante al deber contener a las familias sin conocer si habrán más intoxicados a futuro e insistió en la precaria situación existente en el hospital de Quintero, producto de la distribución de recursos, así como en Loncura, en que el hospital solo cuenta con una posta rural

Agradeció la dotación de profesionales brindados desde las situaciones de emergencia, no obstante, señaló que las medidas implementadas deberían haberse efectuado con anterioridad a los episodios de intoxicación, los que deberían, en su opinión, ser permanentes. Así comento que la finalidad del hospital de campaña no buscaba atender la gran demanda de la comunidad, sino más bien, fue implementado con el objeto de resolver y estudiar los primeros casos de intoxicación advertidos en el mes de agosto, razón por la que especialistas han citado a pacientes para su evaluación durante horario de oficina, con el objeto de practicar exámenes neurológicos, pediátricos, toxicológicos de acuerdo a la gravedad del caso. Añadiendo que las urgencias hospitalarias deben ser atendidas en Urgencias y no en el hospital de campaña.

Expuso la necesidad de practicar estudios desde la óptica de la epidemiología clínica, priorizando a la comunidad en todos sus aspectos, además de asignar de manera permanente condiciones especiales para todas las zonas de sacrificio del país.

Advirtió la necesidad de efectuar estudios toxicológicos que permitan realizar diagnósticos y tratamientos apropiados, además de solicitar la realización de informes que permitan establecer y evaluar todos los factores que inciden en la

contaminación ambiental que afecta la salud, desde un punto de vista multifactorial y multisectorial.

Finalizó expresando que no existe registro sobre las personas que se atienden en el recinto hospitalario de Quintero, ni de aquellos que indican tener domicilio en otras comunas, ya que la mayoría de los pacientes de Quintero se dirigen a los hospitales de Valparaíso o Viña del Mar.

14.- SEÑOR NIELZ CORTÉS, INTEGRANTE DEL CONSEJO PARA LA RECUPERACIÓN AMBIENTAL Y SOCIAL (CRAS) DE QUINTERO Y PUCHUNCAVÍ.

Indicó que tras los eventos de contaminación en las comunas se han desarrollado una serie de organizaciones ciudadanas entre ellas destacó Mujeres en Zona de Sacrificio en Resistencia; Cabildo Abierto de Quintero y Puchuncaví; la Asamblea auto convocada Puchuncaví, y las acciones desplegadas por los sindicatos de pescadores de Horcón, Ventanas, entre otras.

Señaló que se ha confeccionado una serie de exigencias ciudadanas, las que se resumieron en tres puntos: primero, paralización temporal de todo el cordón industrial hasta lograr establecer los responsables; en segundo lugar, la homologación de nuevas normas a las de la OMS para el suelo, el aire y el agua; y en tercer lugar, actualización y modernización de los procesos industriales y cierre de plantas obsoletas.

Sobre el proceso de confección del plan de descontaminación representando por la Contraloría General de la República, indicó que durante la consulta ciudadana la información no estuvo disponible -, es decir, se informaba pero no se leía, por lo que las observaciones ciudadanas se hicieron basadas en el anteproyecto. Terminado el proceso de participación ciudadana se debía generar un informe consolidado con las respuestas, el cual debía hacerse llegar a cada uno de los observantes, pero eso no ocurrió, esa etapa fue saltada y la hicieron después de ser presentado el informe al Consejo de Ministros. En definitiva indicó que no existió participación efectiva de la ciudadanía, toda vez que no se entendieron los antecedentes. Explicó que el anteproyecto es un documento que detalla un cúmulo de valores sin contener mayor información ni explicación alguna, pasando a la regulación a las empresas o las fuentes contaminantes, datos que no permiten ser entendidos sin realizar un estudio en profundidad. Eso sí aseguró que el inventario de emisiones que salió de Valparaíso era diferente al que se firmó en Santiago y que si se comparar la línea base falsa del inventario representado por la Contraloría con el inventario real se favorece con esta diferencia mayormente a Enap.

Sobre la responsabilidad por las intoxicaciones opino que era difícil determinar porque no existen los instrumentos adecuados para hacerlo, y eso es en parte la debilidad como país, se necesitan equipos y nuevas normas. Ejemplificó lo anterior, señalando que existen grandes estanques que acumulan productos químicos; en donde las empresas ventean sus gases o vapores directamente al aire; no existiendo control alguno al respecto, proceso que ocurre en forma automática, es decir, se genera el vapor y se expulsa, advirtiéndose una debilidad en la normativa. Agregó que la Superintendencia del Medio Ambiente carece de recursos necesarios para fiscalizar

Indicó la necesidad de que la evaluación de la normativa ambiental chilena se homologara a las normas de la OMS no tan solo de calidad de aire, sino también de suelo y agua. Entendamos que en Chile no existe una norma de calidad de suelo y de agua, solamente de agua potable. No existe respecto de napas subterráneas y ni siquiera pensar del mar o de fondo marino.

Manifestó que respecto las estaciones de monitoreo, existe la necesidad de cumplir con ciertas calidades, porque hay zonas que tienen poca población, y que perfectamente pudieron haber estado monitoreando, lo que serviría para lograr mejorar la calidad de los antecedentes y datos requeridos.

15.- ROBERTO GONZÁLEZ, PRESIDENTE DE LA UNIÓN COMUNAL DE JUNTAS DE VECINOS DE QUINTERO.

Comenzó señalando que en las comunas de Quintero y Puchuncaví se ha afectado a la población su derecho constitucional de vivir en un medio ambiente libre de contaminación.

Exigió el congelamiento absoluto del parque industrial, catalogándolo de peligroso, contaminante y molesto; la erradicación de termoeléctricas a base de carbón y petróleo; la inmediata homologación de los estándares de contaminantes existentes a las normas de la OMS; la realización de mediciones por un ente sin conflictos de interés; desarrollar acciones con el objeto de lograr la pronta construcción del hospital de Quintero, que le permita satisfacer las complejidades que se presenten e impulsar, a corto plazo, un plan de desarrollo económico y social sustentable para dichas zonas.

Solicitó además, la realización de una exhaustiva investigación que permita identificar las causas y responsabilidades de las empresas por los episodios de contaminación sufridos.

Manifestó la necesidad de contar con propuestas que permitan revitalizar a Quintero y sus alrededores, logrando la sustentabilidad de las ellas mediante el financiamiento de un plan de desarrollo turístico, solicitando la erradicación de contaminación en la zona y los daños ambientales ocasionados.

Relató que en las celebraciones de Fiestas Patrias, producto de la no concurrencia de turistas a la zona, diversos locales comerciales han tenido que dejar de funcionar, lo que ha generado que aproximadamente 100 personas se encuentren cesantes.

16.- SEÑORA ANA ROSA VILLARROEL, CONCEJALA DE PUCHUNCAVÍ.

Se refirió a los pasivos ambientales existentes en las Comunas afectadas e indicó que quedan para siempre y que la responsabilidad era del Estado de Chile por olvidarse de las zonas denominadas de sacrificio, toda vez que el sacrificio significó implementar mayor cantidad de empresas y soportar castigos.

Solicitó que impedir la instalación de empresas en las 500 hectáreas existentes. Expuso que pese a los antecedentes recabados por el gobierno regional y central, al Estado de Chile solo le interesa producir y ganar recursos, sin velar por un desarrollo sustentable, ni por la salud de las personas.

Señaló que si bien los episodios de contaminación disminuirán con el transcurso del tiempo, las intoxicaciones continuarán producto de la contaminación que se produce en la zona, motivo por el que solicitó a las autoridades seguir apoyando a la comunidad, y continuar con las fiscalizaciones, recordando que dichas localidades aportan más del 50% de producto interno bruto a Chile, sin embargo, constituye una comuna pobre.

17.- LUIS PINO, REPRESENTANTE DE LA ASOCIACIÓN REGIONAL DE EXFUNCIONARIOS DE ENAMI.

Cuestionó el premio otorgado por el Certificado de Revisión y Prueba de Caldera (CRCP) a la Responsabilidad social empresarial (RSE) al Puerto Ventanas por la mejor gestión ambiental, evidenciando que en el año 2008 el Puerto Ventanas fue sorprendido contaminando la bahía de Quintero, lo que ocasionó la perdida de fuentes laborales para los pescadores artesanales de la región, y que el Puerto de Quintay se encuentre actualmente contaminado. Señaló que en el año 1985 se denunció de dicha situación, y en el año 1987 la denuncia se realizó por escrito, sin embargo, se hizo caso omiso a sus denuncias.

Manifestó que los certificados de defunción de los trabajadores de Codelco no registran muerte por la contaminación de materiales pesados, sino más bien por cáncer a la vejiga, infarto al miocardio, cáncer al riñón, entre otros. Indicó que algunos cuerpos de trabajadores fallecidos fueron exhumados, advirtiéndose altos niveles de contaminación -huesos, parte del cráneo, costillas-, como el caso del señor Clemente Romero.

Indicó que como fundidor de análisis de oro y plata, controlaban las plantas de la Enami del norte como Chuquicamata, El Salvador, El Teniente y Valdivia, utilizando para dicho análisis el óxido de plomo que es el litargirio, junto con señalar que la empresa Enami no cuenta con las medidas necesarias de seguridad.

Expresó la contaminación de las aguas y que producto de ello los pescadores de Ventanas no podían capturar peces, ya que no existen, producto de la contaminación;

Culminó su exposición solicitando el pago indemnizatorio por los accidentes laborales sufridos y enfermedades producidas en virtud al trabajo desarrollado al interior de la empresa Codelco, además del pago de los finiquitos que actualmente se encuentran impagos.

18.- SEÑOR NOLBERTO DÍAZ, REPRESENTANTE DEL SINDICATO DE LA EMPRESA NACIONAL DEL PETRÓLEO (ENAP).

Reconoció como representante del Sindicato de la Empresa Nacional del Petróleo, la responsabilidad ambiental y de contaminación que afecta a la comuna de Quintero, no obstante, criticó el actuar irresponsable por parte del gobierno, del intendente y de la ministra del Medio Ambiente, toda vez tras concurrir a las instalaciones del terminal Quintero los días 21 y 23 de agosto, le atribuyeron responsabilidad a ENAP, por los episodios de contaminación pese a no encontrar indicios que permitieran concluir aquello. Agregó que la Superintendencia del Medio Ambiente, dos o tres semanas después levantó cargos en contra de ENAP, sin embargo, la comunidad de Quintero está en conocimiento de que ENAP no maneja el terminal Quintero, ya que en dicho lugar se encuentra un terminal de transporte y

de carga de combustibles líquidos, petróleo, o crudo, o refinado, es decir, petróleo natural, petróleo crudo, o productos refinados como bencina, kerosene de avión, que vienen refinados.

Explicó que ENAP mantiene chimeneas en la comuna de Concón, donde actualmente se advierten niveles de contaminación que evidentemente son de su responsabilidad, debido a ello las organizaciones sindicales se opusieron a que se instalara una termoeléctrica de 510 megawatt, gestionada en la gerencia del señor Marcelo Tokman, durante el gobierno de la ex-Presidenta Bachelet. Manifestó además, que dicho proyecto iba a ser realizado a espaldas de la comunidad, en una zona saturada, cuyo financiamiento, la que iba a estar a cargo de ENAP -financiamiento, marca, permiso ambiental e instalaciones en sus terrenos-.

Expresó que la empresa pública, ENAP, siempre se ha hecho cargo de los episodios de contaminación de su responsabilidad, e incluso asumió por los derrames efectuados por los armadores del grupo Von Appen o de la Armada de Chile, ya que tratándose de petróleo crudo distribuido en el mar, sin importar quien efectúe el derrame, responde siempre la Empresa Nacional del Petróleo sea un privado o un público el que haya producido ese derrame. Agregó que como sindicato se opusieron al actuar irresponsable del intendente y del Superintendente del Medio Ambiente, que tras los episodios de contaminación de los días 21 y 23 agosto le atribuyeron responsabilidad únicamente a ENAP.

Agregó, que no desconocen la responsabilidad que le corresponde a ENAP, sin embargo, enfatizó que no es la única empresa responsable de los episodios de contaminación, pese a ello, al tratarse de una empresa pública, debe responder públicamente por las acciones desplegadas. Así, señaló que tras los cierre de estanques efectuado por ENAP luego de los eventos de contaminación ocurridos los días 21 y 23 de agosto en la comuna de Quintero, se han seguido produciendo intoxicaciones.

Manifestó que como trabajadores de ENAP, van a velar por la protección de sus empleos, por lo que expresa su deseo de no cerrar las empresas, no obstante, reconoció que el funcionamiento de las empresas no puede efectuarse a cualquier costo, debiendo regularse el ámbito ambiental y la transparencia, ya que de esa forma se evitaría la corrupción, y recordó la premura -15 días- y el interés del gobierno regional con que se aprobó la ampliación del muelle Oxiquim.

Recordó la situación ocurrida en el año 2009, en que se modificaron por parte del Poder Ejecutivo decretos urbanos que permitieron la instalación de: Campiche, al lado de la comuna de Puchuncaví y de AES Gener. Consideró preocupante que luego de ocurrido ello, no se ponga atención en la responsabilidad de AES Gener, ni a Oxiquim, ni a Gasmar, cuyos ejecutivos vienen de la petrolera estatal, porque casualmente los ejecutivos saltan de un lado a otro, sin ningún control.

Afirmó que a las únicas dos empresas que se les controla es a las estatales ENAP y Codelco, mientras que el resto de las empresas, en manos de privados, no son fiscalizadas, ejemplo de ello, se evidencia en el caso de Oxiquim, GasValpo y de AES Gener. En el caso de GNL Quintero, la empresa apagó su medidor de hidrocarburo durante cinco días, entre el 19 y el 24 agosto y no se ha sancionado por dicha acción.

19.- SEÑOR ALEJANDRO OCHOA, PRESIDENTE DE LA FEDERACIÓN DE TRABAJADORES CONTRATISTAS DE LA EMPRESA NACIONAL DEL PETRÓLEO.

Relató que como representante de los trabajadores contratistas y del sector en el Consejo de Recuperación Ambiental y Social (CRAS), y representante de la Confederación del Petróleo de Chile, hace cuatro años se ha estado trabajando sobre el tema de contaminación existente en las zonas de sacrificio, existiendo actualmente una investigación desarrollada por un grupo de trabajadores de ENAP.

Criticó el actuar de la Seremi de Salud, toda vez que, pese a existir alerta sanitaria por intoxicación, no autorizó la realización de exámenes toxicológicos, además de que las consultas con el toxicólogo son online. Asimismo cuestionó la carencia de medicamentos y la insuficiencia de las medidas del gobierno, las que han sido tardías, como ocurre en el cromatógrafo.

Indicó que la población estuvo y sigue expuesta a un gas que aparece de forma permanente en las mediciones, el metilcloroformo, que fue conocido en el mercado hasta 2017 como tricloroetano. Ese es el nombre químico con que ocultaron el metilcloroformo.

Cuestionó que las autoridades hayan responsabilizado a ENAP en circunstancia de que existen otras empresas más cercanas a la ubicación del Colegio en que se produjo el desmayo de los niños.

20.- SEÑOR ROBERTO MONARDES, PRESIDENTE DE LA AGRUPACIÓN DEL SINDICATO DE PESCADORES ARTESANALES DE LA QUINTA REGIÓN NORTE.

Relató que en la década del 60 se instalaron las primeras 3 industrias, ENAP, Chilectra y Enami, logrando advertirse la contaminación producida luego de 3 años de funcionamiento.

Evidenció que en aquella época existían campos naturales de machas, almejas y ostiones en Loncura, sin embargo, en la actualidad ha disminuido la cantidad de peces y recursos marinos.

Explicó que las industrias comenzaron a instalarse de manera paulatina, comenzando con Enami, la que en principio fue pensada en Los Vilos, sin embargo, se instaló finalmente en Quintero, con el objeto de brindar fuentes de trabajo en la zona de Valparaíso y Quintero.

Relató que los derrames de percloroetileno comenzaron cuando Oxiquim, compró flanches que se rompieron, cayendo al mar 200 litros de percloroetileno, lo que ocasionó la prohibición de desarrollar actividades de pesca y buceo por tres años.

En el año 2008, dentro de las instalaciones de puerto Ventanas, se derramó 2-etilhexanol, químico que recorrió 400 metros del estero Campiche, y al llegar al mar, mató peces, crustáceos y mariscos, sin embargo, el seremi de Salud de aquella época entregó un documento que decía que no había presencia de químicos; sin embargo, el Servicio Nacional de Pesca precisó que el 87% de 2-etilhexanol estaba en el estómago de los peces y el 37 por ciento en las agallas.

Indicó que pese a afirmarse que las empresas cumplen con sus normas, y con las Resolución de Calificación Ambiental (RCA), la realidad es totalmente

distinta, señalando que AES Gener, succionó sardinas, y chungungo el día 10 de septiembre.

21.- SEÑOR JUAN PEÑA, PRESIDENTE DEL SINDICATO CODELCO VENTANAS.

Enfatizó que los trabajadores y de las trabajadoras de Codelco validan y respetan a los movimientos sociales que buscan vivir en un ambiente limpio y sano porque a ellos también les importa ya que viven en estas comunas.

Indicó que en 1990 se permitía emitir 124.000 toneladas de anhídrido sulfuroso sin embargo, actualmente con la dictación del decreto Nº 28 el máximo es 14.000, y Codelco Ventanas emite 10.000.

Señaló que existen más de 35 fiscalizaciones a Codelco Ventanas, sin existir irregularidad alguna. Reconoció que el 23 de marzo de 2011, se experimentó un error operacional, sin embargo, la empresa se responsabilizó se afrontó la situación.

Finalmente solicitó la creación de una nueva normativa, que brinde soluciones y permita cambiar la realidad presente en las localidades de Quintero, Puchuncaví y Concón, implementando a las regulaciones de las empresas, redes asistenciales de calidad, conectividad, de asociaciones, y de programas educacionales, que permitan el reclutamiento de las empresas y llamen a invertir con el objeto de mejorar la calidad de vida de la comunidad.

22.- SEÑOR EZIO COSTA, DIRECTOR EJECUTIVO DE ONG FIMA.

Expuso que la ONG FIMA, es una organización ambiental principalmente dedicada al derecho ambiental y a la defensa de las comunidades en conflictos ambientales.

Indicó que la regulación ambiental chilena está construida sobre la base de instrumentos de gestión ambiental, contempladas en la ley N° 19.300, que entrega, en su opinión, mucha responsabilidad a la administración del Estado, sin embargo ésta es la encargada de regular las cuestiones de fondo. Tal vez por eso, advierte, la administración del Estado, desde el año 1994 ha sido excesivamente lenta y ha omitido la necesidad de regular las cuestiones de fondo en materia ambiental.

En relación con los instrumentos de gestión ambiental que se le entregan al Estado, la ley N° 19.300, esto es, aparte del SEIA, establece el mecanismo de generación de normas de calidad ambiental (primarias y secundarias) y normas de emisión. En todos estos casos se requerirá de un decreto supremo que debe seguir ciertos pasos para su elaboración y establecer su contenido normativo. Así se dicta en el año 2002 la norma de calidad primaria de aire para dióxido de azufre (SO2)

Supuestamente, las normas de calidad y las normas de emisión debieran ser revisadas de manera periódica para los efectos de actualizarlas al conocimiento científico, por una parte, y por otra, eventualmente, ir aumentando el grado de protección de la población y del medio ambiente, sin embargo la norma SO2, de 2002, no ha sido actualizada por el Ministerio del Medio Ambiente, sin perjuicio de lo cual se comenzó un proceso de actualización que comenzó en 2010 y terminó en 2017, y en ese año el Consejo de Ministros para la Sustentabilidad aprobó una nueva norma de SO2, que todavía no se publica en el Diario Oficial. Agregó que se interpuso un

recurso de protección por esta omisión y el Ministerio del Medio Ambiente contestó que la norma había sido aprobada a fines de 2017, pero sin la firma de la Ministra de Salud de la época, sin dar razones.

Mencionó que esta norma de SO2 es una de las pocas que existen, en materia de protección del aire. En materia de protección de suelo, no existe ninguna norma, y en materia de protección de agua, existen algunas, que son dispersas en algunos cuerpos de agua de Chile.

Consideró particularmente importante, en el caso de Quintero Puchuncaví, que existan normas en un futuro respecto de los compuestos orgánico volátiles, que son los contaminantes que provienen principalmente de los hidrocarburos, por lo tanto, de los procesos industriales que se llevan a cabo en la zona, y que existan normas de suelo particularmente respecto del arsénico, que es un elemento conocidamente contaminante, un metal pesado que se va acumulando en el cuerpo de las personas, y produce una serie de enfermedades muy graves. Asimismo en esta zona existe acumulación de arsénico en el suelo, medida en distintos estudios, muy por sobre lo recomendable para la vida saludable de las personas. Agregó que este contaminante proviene principalmente de la actividad de las termoeléctricas, en especial de las termoeléctricas a carbón, que está presente en todas las zonas de sacrificio de Chile.

Explicó que un segundo instrumento de gestión ambiental son los planes de prevención y descontaminación, sin embargo consideró que generalmente se quedan cortos en su configuración regulatoria, pues sólo se hacen cargo de aquellos contaminantes que están normados. En el caso de Quintero-Puchuncaví del SO2, del MP-10, del MP-2.5, pero además se abarca esos contaminantes en los niveles que las propias normas hayan establecido, porque la idea de los planes es que se vuelva a los niveles anteriores a la saturación. Por lo tanto, si las normas son pocas y además poco exigentes, la vuelta al estándar de la norma no significa, de ninguna manera, un mejoramiento de la calidad del medio ambiente. Por lo tanto, el plan de prevención y descontaminación, no logra prevenir ni descontaminar una zona que tiene una serie de contaminantes distintos a los que están normados, y que, además, si volviera a los niveles previos, se encontraría igualmente contaminada.

Comentó que el gran instrumento de gestión ambiental en Chile es el Sistema de Evaluación de Impacto Ambiental y que analizando las causas que han llevado a que existan las zonas de sacrificio, postuló que:

1) La no evaluación ni fiscalización de proyectos antiguos, esto es, aquellos construidos en forma previa a la entrada en vigencia de la Ley 19.300 sobre Bases Generales del Medio Ambiente, y que por tanto no tuvieron que evaluarse en el Sistema de Evaluación de Impacto Ambiental (SEIA). Explicó que no se han evaluado a pesar de que la ley N° 19.300 no consagra dicho principio, sin embargo, existe un principio de gradualidad que señala que la normativa ambiental se debe ir aplicando gradualmente. Sin embargo consideró impresentable que en grandes complejos industriales una pequeña parte de tecnología nueva, que es la menos contaminante, sí está evaluada, y otra gran parte de tecnología antigua, que es la más contaminante, no lo esté. Precisó que no existen razones jurídicas para la no evaluación y en este punto ha existido una omisión del Servicio de Evaluación Ambiental, que mediante la interpretación de algunas de las normas de la ley N° 19.300, debió forzar, provocar o, por lo menos, incentivar que se evalúen los proyectos antiguos. A diferencia de Perú en que se han considerado ciertos

instrumentos de gestión ambiental específicos para la evaluación de proyectos antiguos.

2) La no actualización de resoluciones de calificación ambiental (RCA), Esto es relevante porque las calificaciones ambientales están hechas sobre una base fáctica que va cambiando en el tiempo. Lo que se evalúa de un proyecto es la línea de base que presenta el titular en el momento de instala en un lugar, sin embargo las condiciones ambientales, sociales, etcétera, de ese lugar, van cambiando en el tiempo. Añadió que esa posibilidad de revisión, debió haber sido utilizada por el Servicio de Evaluación Ambiental, y particularmente cuando en la modificación de la ley N° 19.300 se forzó que la evaluación considerara los efectos sinérgicos y acumulativos, que antes no se evaluaban.

Concluyó refiriéndose a la fiscalización como instrumento de gestión ambiental. Indicó que existe un gran problema en la construcción de la potestad de la Superintendencia de Medio Ambiente, ya que solo puede fiscalizar las Resoluciones de Calificación Ambiental y, como se observó antes, existen falencia en los planes de prevención y contaminación, en las normas de emisión y en las normas de calidad, es decir que la Superintendencia se queda sin qué fiscalizar, aun existiendo un daño ambiental o un daño a la salud, no tiene cómo investigar a partir del daño sino que debe ir a investigar a los que estima que podrían ser los productores del daño y fiscalizarlos en base a los permisos que esos posibles productores del daño tendrían.

23.- SEÑORA FLAVIA LIBERONA, DIRECTORA EJECUTIVA DE LA FUNDACIÓN TERRAM.

Comentó que la justicia ambiental aparece en la historia mundial como un mal menor cuando opciones de desarrollo se instalan en los territorios y en ellos se sitúa externalidades negativas con lo que se inicia la desigualdad y nace el concepto de justicia ambiental.

En el caso particular de Chile este tema es de larga data, sin embargo, hay un hito en la legislación ambiental y es que en el año 1994, el entonces Presidente Frei, al poner la primera piedra de la Central Pangue, dijo que ningún proyecto se detendrá por consideraciones ambientales. Esto incidió en la forma cómo se ha desarrollado lo relativo a la institucionalidad ambiental, particularmente en Puchuncaví y Quintero.

El derecho a vivir en un medioambiente libre de contaminación es un derecho humano e interdependiente de otros derechos y desde esta perspectiva es analizado por todas las organizaciones de derechos humanos, incluido el Instituto de Derechos Humanos en Chile.

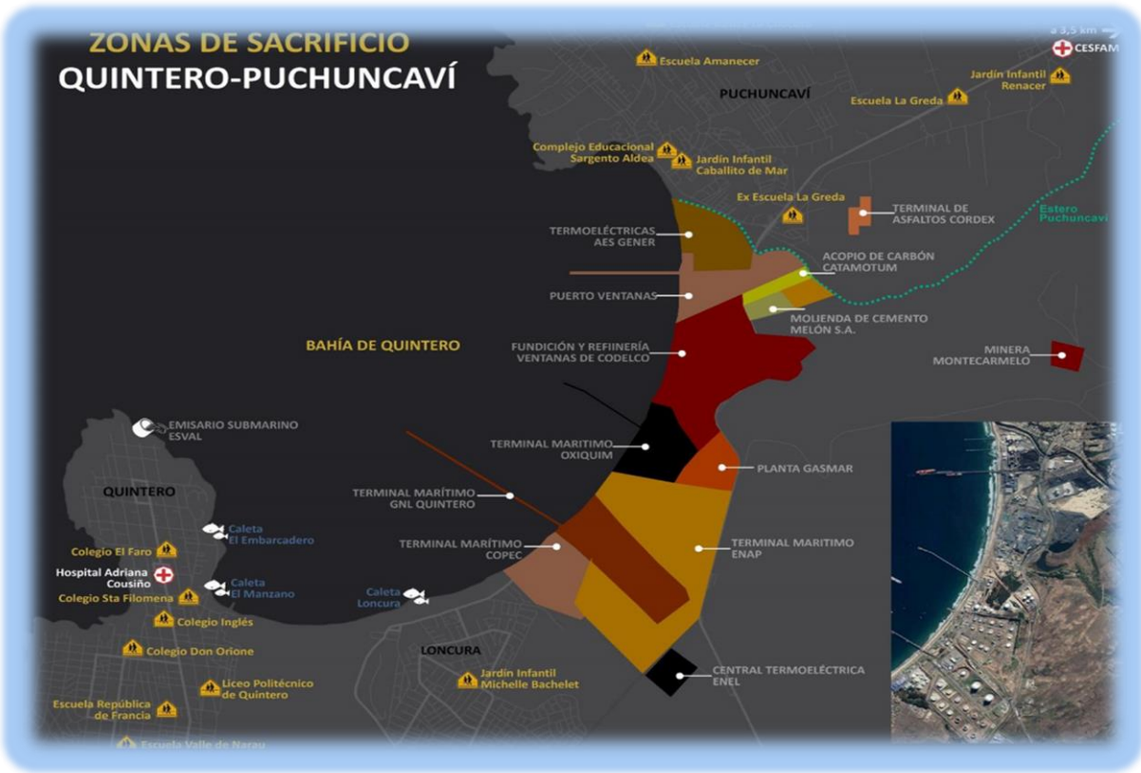
No obstante, en las zonas de sacrificios se vulneran varios derechos humanos, como el derecho a vivir en un medioambiente libre de contaminación, el derecho a la vida, a la salud, a la educación, etc.

Señaló que en Chile se han identificado 5 zonas de sacrificio: Tocopilla, Mejillones, ambas en la región de Antofagasta, Huasco, Puchuncaví-Quintero y Coronel, y que una sexta que también puede suscribir a ese concepto es Til Til.

Apuntó que la ley sobre Bases Generales del Medio Ambiente es del año 1994 y el reglamento es del año 1997, por lo tanto los proyectos que entraron en

operación antes de 1997 no cuentan con Resolución de Calificación Ambiental (RCA) y eso incide en que la Superintendencia no pueda fiscalizar. Asimismo destacó las pocas normas existentes en materia ambiental, como la de calidad, la de emisión, pocas normas de aguas e inexistente norma para evaluar la contaminación en suelos.

Así en el parque industrial de Quintero-Puchuncaví existen industrias que no tiene Resolución de Calificación Ambiental. Y por lo tanto la Superintendencia no puede fiscalizar, y si estas industrias que están operando no cuentan con RCA en su operación principal difícilmente se sabrá lo qué pasó o qué puede pasar en esta zona. Por ejemplo Puerto Ventanas empieza a operar en 1991 y cuenta con 6 Resoluciones de Calificación Ambiental, todas por declaración de impacto ambiental, y ninguna de su operación principal.



Consideró importante revisar las Resoluciones de Calificación Ambiental de la bahía de Quintero y determinar a ciencia cierta cuántas industrias cuentan con Resolución de Calificación Ambiental sobre sus operaciones principales y solicitar información sobre cuántos proyectos han sido modificados vía pertinencia, porque dicha pertinencia no se hace parte de la Resolución de Calificación Ambiental; no queda en el expediente público del SEA y no es fiscalizable por la Superintendencia.

Industrias sin evaluación ambiental del proyecto principal

INDUSTRIA	CONTROLADOR	SECTOR PRODUCTIVO	INICIO OPERACIONES	RCA			
				AÑO	PRESENTACIÓN	Continuación AÑO	Continuación PRESENTACIÓN
Puerto Ventanas	AES Gener/Panimex Química S.A.	Infraestructura Portuaria	1991	2000	DIA	2010	DIA
				2004	DIA	2014	DIA
				2005	DIA	2015	DIA
Terminal Marítimo de Quintero ENAP	ENAP	Infraestructura Portuaria	1954	2000	DIA	2005	DIA
				2001	DIA	2006	DIA
				2002	DIA	2009	DIA
				2002	DIA	2009	DIA
				2004	DIA		
Fundición y Refinería Ventanas	Codelco	Instalación fabril	1964	1998	DIA	2009	DIA
				2003	DIA	2010	DIA
				2004	DIA	2011	DIA
				2005	DIA	2013	DIA
				2007	DIA	2016	DIA
				2008	DIA		
Terminal Marítimo de Quintero Copec	COPEC S.A.	Infraestructura Portuaria	2006	1999	DIA	2005	DIA
				2002	DIA	2008	DIA
				2003	DIA	2013	DIA
				2007	DIA	2014	DIA
				2004	DIA		
Planta Gasmar Quintero	Gasmar	Transportes y almacenajes	1992	2005	DIA		
				2013	DIA		
Terminal Marítimo Oxiquim	Oxiquim S.A.	Infraestructura Portuaria	1990	1999	DIA	2007	EIA
				1998	DIA	2009	DIA
				1998	DIA	2013	DIA
				2005	DIA	2013	EIA
				2007	DIA		

INDUSTRIA	CONTROLADOR	SECTOR PRODUCTIVO	INICIO OPERACIONES	RCA			
				AÑO	PRESENTACIÓN	Continuación AÑO	Continuación PRESENTACIÓN
Planta de procesamiento de sales metálicas	Minera Montecarmelo S.A.	Minería		2004	DIA		
Planta de Molienda de Cemento Puerto Ventanas	Melón S.A.	Instalación fabril	2011	2005	DIA		
				2006	DIA		
				2007	DIA		
Comercial Catamotum	Catamotum S.A.	Chancado de Carbón		Sin RCA			
Complejo Termoeléctrico Ventanas	AES Gener	Energía	1964	2001	DIA	2008	DIA
				2006	EIA	2010	EIA
				2006	DIA	2011	EIA
				2007	DIA		

Industrias con evaluación ambiental del proyecto principal

INDUSTRIA	CONTROLADOR	SECTOR PRODUCTIVO	INICIO OPERACIONES	RCA			
				AÑO	PRESENTACIÓN	Continuación AÑO	Continuación PRESENTACIÓN
Terminal Marítimo GNL	GNL Quintero S.A.	Infraestructura Portuaria	2009	2005	EIA	2012	DIA
				2007	DIA	2013	DIA
				2008	DIA	2014	DIA
				2009	DIA	2016	EIA
				2010	DIA		
Central Quintero	ENEL/ex Endesa	Energía	2009	2007	DIA	2009	DIA
				2008	EIA	2010	DIA
Terminal de asfaltos y combustibles	Cordex S.A.	Infraestructura Portuaria	1998	1998	EIA		

En este punto consideró indispensable que la Superintendencia del Medio Ambiente informe sobre sus reales capacidades de fiscalización,

Por otra parte, indicó que el Ministerio del Medio Ambiente dicta normas primarias o secundarias de calidad y normas de emisión. Estas normas, al igual que los planes de descontaminación, deben ser revisadas cada cinco años. Sin embargo, no existe un sistema de priorización de normas y así se da el caso del DS N° 90, que establece la norma de emisión para la regulación de contaminantes asociados a las descargas de residuos líquidos a aguas marinas y que se encuentra en revisión hace 12 años.

La ley N° 19.300, sobre Bases del Medio Ambiente define contaminación como la presencia en el ambiente de sustancias, elementos, energía o la combinación de ellos en concentraciones y permanencia superiores o inferiores, a las establecidas en la legislación vigente, no obstante si no hay normas no hay contaminación.

Sobre la escasa normativa ambiental, sostuvo que no existe norma primaria de calidad de arsénico, de compuestos orgánicos volátiles, de compuestos orgánicos persistentes, de suelos, de agua, de contaminación difusa, etcétera. Indicó la urgencia de contar con una normativa de calidad primaria de arsénico respirable que fue derogada en el año 1994.

Sugirió que se realicen estudios de aguas de pozo, para saber si están contaminados o no, ya que en Puchuncaví la población toma agua de pozo

Concluyó que, por los episodios de intoxicación recién ocurridos, así como lo pasados en la escuela La Greda, se debe solicitar un sistema de monitoreo ambiental en los colegios.

24.- SEÑORA PATRICIA MUÑOZ, DEFENSORA DE LA NIÑEZ.

Manifestó que para la Defensoría de la Niñez, en relación con la población objetiva de niños, niñas y adolescentes de la zona, existen tres derechos fundamentales que están siendo gravemente vulnerados: el derecho a la vida, el derecho a la integridad física y psíquica, y el derecho a vivir en un medio ambiente libre de contaminación, sin que el Estado tome medidas al respecto ni menos para instaurar una solución eficaz.

Indicó que desde el punto de vista de la intervención estatal, y el rol de los distintos agentes del Estado, el principio precautorio obliga al Estado a no justificar una inacción basada en la desinformación de los agentes que están generando la situación conflictiva. En razón de ello indicó que se solicitó el cese absoluto de la faena industrial de todas las empresas del cordón industrial de Quintero y Puchuncaví, toda vez que no existe posibilidad de determinar cuáles son los agentes provocadores de las intoxicaciones en las personas que viven en dichas localidades, y especialmente, en el caso de niños, niñas y adolescentes.

Manifestó que es necesario determinar la manera en la que el Estado de Chile, a través de sus organismos competentes, ejerce el principio precautorio, desplegando acciones tendientes a evitar mayores perjuicios a la salud de las víctimas y de aquellos que residen en la zona.

Recordó que con fecha 31 de agosto se evidenciaron 408 personas con síntomas de intoxicación, constatándose tras la visita que al menos en dos jardines infantiles - Bambi, de Quintero y Arboleda, de Puchuncaví-, había niños preescolares con síntomas de intoxicación, advirtiéndose la gravedad de la situación.

Manifestó que recién el día 10 de septiembre el Estado tomó el control de la situación, pero en términos de supervisión como lo fue el control efectivo de monitoreo y que la Superintendencia de Medio Ambiente solo puede intervenir en aquellas empresas que cuentan con la Resolución de Calificación Ambiental (RCA), y en consecuencia carecen de toda intervención y procesos sancionatorios las que no tienen RCA.

Expresó que no existe certeza sobre las causas de contaminación ni control de las autoridades de la Superintendencia del Medio Ambiente, del Ministerio del Medioambiente y del Ministerio de Salud frente a los eventos contaminantes. En este sentido agregó que las autoridades locales y nacionales no cuentan con instrumentos que permitan determinar los agentes contaminantes, ni existe un sistema de monitoreo integral, de acuerdo a lo declarado por la propia Ministra del Medio Ambiente ante esta Comisión, quien además sostuvo que el sistema de monitoreo existente tenía carácter de propio y privativo de las empresas, las que se auto fiscalizan y además, recordando los dichos de la Ministra del Medio Ambiente que los medidores en manos de las empresas sólo miden gases normados.

Asimismo indicó que, de acuerdo a lo señalado por la Ministra de Medioambiente y el Superintendente Cristián Franz, las reglas de medición son insuficientes para garantizar el derecho a la salud y a la vida e integridad física de los habitantes de la zona, producto que los niveles de exigencia se realizan en promedio por día y año. Explicó que estos niveles permiten que de manera legal, se mantengan durante horas los altos niveles, para posteriormente disminuirlos hasta llegar a cumplir con los promedios.

Argumentó que si se revisan las concentraciones existentes en las estaciones de monitoreo de calidad del aire, se observará que sistemáticamente, -no solo los días 3 y 4 ni los últimos 3 o 4 años, desde la fundición se ha producido *peak* de SO2, de dióxido de azufre, el que es considerado como veneno para la salud humana, de acuerdo a lo definido por el Ministerio del Medio Ambiente.

Advirtió que la única acción, por parte del Estado, que permitiría controlar la situación, y en consecuencia lograr evitar que la ciudadanía siga sufriendo episodios de intoxicación, es el cese de la faena industrial, mientras no se pueda determinar a los agentes provocadores de intoxicación. Agregó que además, es necesaria una intervención sanitaria con una reglamentación que determine los límites de tolerancia de los agentes químicos y contaminantes en la población que limite la actividad industrial. Y también establecer normas ambientales que determinen la forma de control y de fiscalización.

25.- SEÑOR OSVALDO TORRES, JEFE DE LA UNIDAD DE ESTUDIOS DEL INSTITUTO NACIONAL DE DERECHOS HUMANOS.

Expuso que una de las recomendaciones efectuadas en el informe de la misión-observación, que se realizó entre el 11 y 13 de septiembre, fue facilitar a la población una información clara respecto a las medidas preventivas que deben adoptar y sobre lo que efectivamente ocurre en las zonas afectadas por contaminación.

Indicó que la segunda recomendación dice relación con promover, alrededor del acceso de la información, prácticas de información, de participación pública y de acceso a la justicia en los asuntos ambientales, con el nivel de los estándares internacionales, mencionando el Acuerdo de Escazú, como norma que establece adecuados estándares para acceder a una buena información, la que además, está fuertemente relacionado con el tema de la justicia por parte de los afectados, respecto a la vulneración de derechos.

Recomendó en tercer lugar efectuar mediciones de contaminación de aire, suelo y aguas, incluso revisar el estado del agua que se consume en las localidades, toda vez que se cuestiona su potabilidad.

En virtud de lo anterior, manifestó la necesidad de informar a la población sobre lo que está ocurriendo, y contar con información sobre las mediciones efectuadas de acuerdo a lo declarado por el Presidente de la República durante su visita en la zona.

Expuso como cuarta recomendación efectuar de manera planificada y gratuita los exámenes toxicológicos necesarios para determinar con mayor certeza e imparcialidad la existencia de contaminantes presente en los cuerpos de los habitantes de la zona. Agregó que ello se asocia al tema ocurrido en el cerro Chuño, en Arica, donde se instaló una población sobre un cerro lleno de desechos de plomo de los años 80, y luego de un tiempo comenzaron a sufrir una serie de afectaciones, lo que motivó a la aprobación de una ley específica.

Señaló como quinta recomendación, la implementación de un sistema de monitoreo permanente de las condiciones de salud de la población, pues realizar un examen sólo una vez no permite determinar con claridad la fuente de contaminantes ni los productores directos de ella.

Expresó como sexta recomendación, implementar un sistema de medición de emisiones, el que debe ser monitoreado de manera independiente, con autonomía técnica permanente, efectiva y veraz, además de contar con la participación de miembros de confianza a la comunidad y en lugares adecuados.

Advirtió el sentimiento de sospecha y desconfianza existente en la población, la que lleva a plantear la idea de efectuar una medición que se realice mediante la participación de miembros de la comunidad, que no significa entregar dicha labor a la comunidad, sino que a sujetos de confianza y con conocimiento técnico. Junto con ello, mencionó que los monitoreos deben efectuarse en lugares adecuados, en los que se midan la real afectación de las emisiones.

Indicó como séptima recomendación, la implementación de un nuevo plan de descontaminación, cuya aprobación está comprometida para diciembre próximo.

Sostuvo como octava recomendación, proponer medidas de contingencia respecto de la situación escolar, para posteriormente efectuar la redacción de informes, sobre apoyo a los escolares para la rendición de la PSU, debiendo analizarse además las solicitudes efectuadas por las movilizaciones estudiantiles.

Explicó que la novena recomendación tiene que ver con la generación de la figura del delito ambiental, la que permita atribuir responsabilidades concretas.

Señaló que la décima recomendación solicita incorporar y persuadir a las empresas para que se hagan parte de los Principios Rectores de Naciones Unidas de Empresas y Derechos Humanos. Agregó que en Chile pese a existir el Plan de Acción Nacional de Empresas y Derechos Humanos no se ha avanzado en esa dirección. Los principios rectores obligan al Estado a que todas las empresas públicas respeten los derechos humanos, por ende, deben respetar el derecho a vivir en un medioambiente libre de contaminación y en ese sentido actuar con debida diligencia para prevenir, mitigar y reparar los daños causados por una acción indebida o vulneradora de derechos.

Indicó como decimoprimera recomendación, prestar atención a las labores desplegadas por Fuerzas Especiales de Orden y de Seguridad Pública en la zona, con el objeto de cautelar el derecho de los habitantes a manifestarse de manera pacífica, argumentando que de acuerdo a las opiniones recogidas por los locatarios, ha existido un exceso de presencia policial y de uso de fuerza, como ocurrió en el caso del muelle en Quintero, donde funcionarios de la Armada de Chile participaron en actos de represión.

Planteó como decimosegunda recomendación, la idea de modificar los actuales instrumentos que rigen el ordenamiento territorial de la zona, particularmente el Plan Regulador Metropolitano-Valparaíso, congelando la autorización de inversión en las 754 hectáreas aún disponibles para actividades peligrosas. Asimismo, mencionó considerar una modificación al actual Sistema de Evaluación Ambiental, toda vez que el control de las emisiones es realizado por cada unidad de emisión y no por el impacto, o la sinergia producida por el conjunto de instalaciones de la zona que emiten hacia el suelo, el agua y el aire.

26.- SEÑOR FERNANDO MARTÍNEZ, JEFE REGIONAL DEL INSTITUTO NACIONAL DE DERECHOS HUMANOS.

Explicó que si bien los episodios de contaminación conocidos comenzaron el 21 de agosto, en los últimos 10 años, desde 2008, se han producido al menos nueve episodios de contaminación, con un menor número de personas afectadas, no obstante, han alcanzado distintos niveles de gravedad, siendo el más conocido, el episodio de la escuela La Greda. Agregó que producto del incumplimiento del Estado del deber de garantizar el vivir en un medioambiente libre de contaminación se ha generado este problema ambiental, lo que ha llevado a la Institución a presentar un recurso de protección por infracción al derecho a vivir en un medioambiente libre de contaminación y por la infracción al derecho a la integridad física y síquica de las personas. Agregó que en este contexto, se ha solicitado que el Estado adopte todas las medidas necesarias para revertir el proceso sufrido, y asegurar la tutela de los derechos fundamentales vulnerados.

Indicó la necesidad de realizar exámenes toxicológicos que hasta la fecha no se han realizado, además, de realizar un monitoreo permanente de la situación de salud de las personas que hasta ahora han resultado afectadas, como así también, recabar información exacta sobre la cifra de personas dañadas, ya que de acuerdo con los números entregados por el hospital de Quintero, la directora mencionó una cifra cercana a las mil atenciones por intoxicaciones.

Solicitó determinar las responsabilidades administrativas, estableciendo la autoridad específica a la que le corresponde atribuir la responsabilidad por los hechos producidos, sin embargo hizo presente que en los nueve episodios registrados en los últimos diez años, hubo reacciones de distinto tipo por parte de autoridades del Estado, no obstante, el problema no se ha solucionado.

27.- SEÑORA ALEJANDRA DONOSO, DIRECTORA EJECUTIVA DE LA DEFENSORÍA AMBIENTAL

Sostuvo que en un informe del año 2014, el INDH reconoció la existencia de cinco zonas de sacrificio en el país en un capítulo completo referido a esta situación, señalando que el concepto de “zonas de sacrificio” permite dar cuenta de una situación ya constatada: la concentración de los costos ambientales y su distribución desigual. Es una situación de injusticia ambiental evidente, por cuanto los beneficios que genera una industria se reparten difusamente entre la sociedad toda, mientras que los costos ambientales son soportados por personas en situación de vulneración social y económica.

Mencionó que en mayo de 2014, la Unión de Comunas de Zonas de Sacrificio emitió un pliego de peticiones al Estado donde las define como “aquellos territorios de asentamiento humano devastados ambientalmente por causa del desarrollo industrial. Esta devastación tiene implicancias directas en el ejercicio pleno de los derechos fundamentales de las personas; derecho a la vida, a la salud, a la educación, al trabajo, a la alimentación, a la vivienda, etc. En estos territorios el daño ambiental ha significado la situación de vulnerabilidad y empobrecimiento de las comunidades”.

Hizo presente que se han identificado tres causas principales que explican que en Chile existan “zonas de sacrificio”, todas ellas redundan en un diagnóstico inequívoco: un diseño normativo obsoleto.

En primer lugar, hay una regulación deficiente, que no entrega elementos de control para la presencia de elementos reconocidamente dañinos para la salud de las personas. Por una parte, existe un pequeño número de elementos contaminantes normados (MP10, MP 2,5, SO2, NOx, O3), pero con un estándar muy inferior al recomendado por la OMS. Por otro lado, existe un gran universo de sustancias contaminantes que no tienen regulación (Cd, Cr, Pl, Cu, Zn, etc.). Consideró especialmente grave que Chile no tenga norma de calidad de aire para arsénico, así como también la inexistencia de normas para los contaminantes fugitivos, ni para los compuestos orgánicos volátiles (COV) que emanan de los hidrocarburos.

Mencionó que la gravedad de esta situación radica en que, por una parte se trata de contaminantes nocivos para la salud, cuyo contacto con la vida humana genera enfermedades agudas y crónicas que afectan, principalmente, los sistemas respiratorio, cardiovascular y nervioso y, por otra parte se trata de contaminantes presentes en las denominadas zonas de sacrificio, que son parte de las emisiones de los procesos productivos de las industrias instaladas, muchas de las cuales se originan en la combustión de sustancias fósiles y altamente tóxicas, como el carbón.

Se acentúa el riesgo por los efectos sinérgicos y acumulativos de dichas emisiones, los que se explican por un inadecuado uso de los instrumentos de planificación territorial y de gestión ambiental, generando una ausencia de límites en la permisividad de instalaciones industriales.

En el caso de Concón, Quintero y Puchuncaví, el complejo industrial data de 1964, muchas de las industrias instaladas en esa época continúan vigentes (Codelco, Aes Gener, Puerto Ventanas). Muchas de las instalaciones no fueron evaluadas ambientalmente; otras tantas han sido modificadas y evaluadas sólo parcialmente. Lo más preocupante son las innumerables modificaciones que se han hecho por la vía de las cartas de pertinencia, sin entrar a evaluación ambiental.

Aseguró que los instrumentos de planificación territorial tampoco se hacen cargo de una política de ordenamiento territorial que respete los derechos de las personas, pues permite la instalación de grandes núcleos industriales, generadores de amplias externalidades negativas, en lugares excesivamente cercanos a la población.

Esta situación redunda en una desprotección de los bienes jurídicos que el Estado está llamado a proteger. Expresó que en las zonas de sacrificio no se resguarda adecuadamente el derecho a un medio ambiente sano, ni la integridad física y psíquica de sus habitantes. Los episodios de envenenamientos masivos ocurridos en Quintero y Puchuncaví desde el 21 de agosto dan cuenta de ello. En su opinión la población se envenena por respirar, sin saber cuál es el origen específico, ni el gas de que se trata ni los tratamientos adecuados.

Agregó que todo esto redunda en un diseño normativo obsoleto, que no protege al bien jurídico medio ambiente, que impone la instalación de industrias contaminantes por vías que no aseguran un adecuado análisis de los impactos ambientales que se generarán ni la exigencia de medidas idóneas de mitigación, reparación o compensación, y que se instala sin la participación de los habitantes que soportarán las externalidades negativas, sumado a ello sin contar con una correcta fiscalización por la Superintendencia de Medio Ambiente

Indicó que se mantiene un sistema que no reporta suficiente información para hacer frente a las cada vez más frecuentes crisis ambientales y sanitarias, mermando la posibilidad de ejercer los derechos de acceso a la justicia ambiental para la población afectada, fallando así el Estado en su deber de promoción y protección de los derechos humanos.

Sólo a modo de ejemplo, señaló que entre el 1 de enero y el 20 de agosto de 2018, en las comunas de Quintero y Puchuncaví hubo 2 derrames de petróleo, 8 episodios de intoxicación masiva, 25 varamientos de carbón y 26 peaks de SO2.

Sostuvo que en las zonas de sacrificio los derechos a la vida e integridad física y psíquica, salud adecuada y medio ambiente sano, no pueden ser ejercidos adecuadamente. Así lo ha entendido el Relator Especial sobre los derechos humanos y el medio ambiente de la Oficina del Alto Comisionado de Naciones Unidas quien ha dicho que: “sin un medio ambiente saludable, no podemos hacer realidad nuestras aspiraciones, ni siquiera vivir en un nivel acorde con unas condiciones mínimas de dignidad humana.”

Luego, en específico, la respuesta institucional ante la emergencia sanitaria por causa de envenenamientos masivos por gases tóxicos, ha vulnerado los derechos a la vivienda, la educación, la niñez, la cultura y económicos, por mencionar los más evidentes.

Señaló que la respuesta que da el ordenamiento jurídico a esta problemática es insuficiente e inadecuada, llegando a ser incluso injusta. Así explicó que instituciones como la prescripción pueden jugar en contra de la responsabilidad por los daños ocasionados, los que son íntegramente soportados por una comunidad que, en caso de buscar justicia institucional, debe probar la ilegalidad de la fuente de la contaminación, en un contexto de excesiva permisividad por parte del Estado, además debe probar la significancia de un daño que tiene características de sinergia y acumulación muy difíciles de caracterizar, e incluso debe demostrar específicamente cuánto porcentaje de la contaminación produce cada una de las posibles fuentes, y cuánto de ese porcentaje afecta a cada elemento del medio ambiente dañado, incluida la salud de las personas. En otras palabras, se pretende que las personas afectadas conozcan a ciencia cierta el contaminante que les está afectando y quién lo produjo.

Esta distorsión del ordenamiento jurídico es incompatible con una situación de “zona de sacrificio” donde los derechos de acceso a la información, participación y justicia ambiental están ausentes, jugando el estándar probatorio establecido a favor de la perpetuación y profundización de la injusticia ambiental.

28.- SEÑORA JUANITA FERNÁNDEZ, PRESIDENTA DE LA COMISIÓN DE MEDIO AMBIENTE Y DERECHOS HUMANOS DEL COLEGIO MÉDICO DE VALPARAÍSO.

Explicó que descontaminar es eliminar o, al menos, disminuir la contaminación. Si se piensa que el objetivo de un plan de descontaminación es solo cumplir una norma, se debe aclarar a qué norma se hace referencia, porque –curiosamente- todas las empresas cumplen con la norma. Esto ocurre, porque se habla de dos normas distintas: una es la norma de emisión, el permiso que tiene cada empresa, y, la otra, es la norma que es el resultante de eso, porque comparten el mismo espacio aéreo. Por lo tanto, no se puede hablar de normas de emisión cuando se habla de contaminantes, que son dañinos para la salud.

Ejemplificó lo dicho diciendo que si a esta sala ingreso un auto, que tiene sello verde y que, por ende, no emite muchos contaminantes, está bien. Pero si a esta misma Sala ingresamos 18 autos, no podemos guiarnos porque cada uno tenga el sello verde al día, sino por el resultado que eso va a dar para el aire que estaríamos respirando todos los presentes.

Afirmó que una de cada tres muertes por cáncer pulmonar es producida por el asesino invisible, que es la contaminación. Un cuarto de los accidentes vasculares encefálicos, un cuarto de las enfermedades al corazón, un cuarto de las enfermedades bronquiales obstructivas crónicas, todas son causadas por el asesino invisible.

De ahí que sostuvo que no se está respetando el derecho a vivir en un medio ambiente libre de contaminación, ni el derecho a la protección de la salud, ni el de igualdad ante la ley.

Indicó que la gente no sabe que el material particulado por sí y separado del PM2.5 son los dos factores cancerígenos para los seres humanos en grupo 1, y el riesgo es directamente proporcional al año de exposición y a las dosis. Mencionó que antiguamente, se había declarado asociación entre componentes de polución y cáncer, como los gases del diésel, pero, desde 2013 en adelante, se sabe que son hechos causales. El factor causante de mayor daño es el PM2.5.

Comentó que en los meses de mayo, junio y julio, se habló de la importancia de los compuestos orgánicos volátiles, porque sabían que en Concón, especialmente, y en la zona de Quintero se estaban emitiendo compuestos de xileno, tolueno y benceno. De hecho, uno de los componentes que se encontró, de los cuatro citados por el Seremi luego de la intoxicación del 21 de agosto, fue precisamente nitrobenceno que tiene olor almendrado parecido al gas prúsico de las cámaras de gases, pero no era ese. Tiene un efecto neurológico, razón por la cual sospechamos que hubo orgánicos volátiles dando vueltas.

Hizo presente que los médicos todavía no saben qué fue lo que se emitió al aire. Hay empresas que emitieron algo y no han dicho qué es. No obstante que debería hacerse énfasis en la responsabilidad de las empresas, en cuanto a revelar lo que, efectivamente, han eliminado al ambiente.

Precisó que el MP2.5 es muy pequeño que es el más dañino porque llega directo al torrente sanguíneo y, según su composición, puede producir diferentes patologías. Los contaminantes mayores son: PM10, PM2.5, ozono, dióxido de nitrógeno, dióxido de azufre, metales pesados y VOC o COV.

Recordó que respecto del PM2.5, el promedio anual que dice la OCDE es de 2 microgramos por metro cúbico y con 10 microgramos por metro cúbico se permite el doble; el promedio de 24 horas del PM2.5, se permite dos veces el doble; el PM10, dos veces y media; el promedio 24 horas, tres veces; el O3, 1.6 veces.

Sostuvo que el NO2 es uno de los factores más importantes para producir ozono, que se produce por la exposición del NO2 con los rayos ultravioletas. Se produce esta interacción química y se libera O3, que es el ozono. El ozono es sumamente irritante, es muy dañino para la salud, especialmente en el área pulmonar.

Respecto del dióxido de azufre, el promedio de 24 horas que toleramos en Chile es 12 veces y media de lo que señala la norma internacional. Además no existen normas sobre calidad de suelos. En efecto hay contaminantes que no permiten la vida como el hidrocarburo y no hay normas, y si se construye ahí, la gente se va a morir.

Tampoco hay normas de compuestos orgánicos volátiles; ni normas de calidad de aire de arsénico, que es un cancerígeno en todo el mundo.

Indicó que en Chile se tienen normas anormales, porque no es normal que un país de la OCDE tenga las peores normas: tenemos 46 microgramos por metro cúbico de material particulado cuando el promedio en la OCDE es de 20 microgramos por metro cúbico.

29.- SEÑOR ANDREI TCHERNITCHIN, PRESIDENTE DEL DEPARTAMENTO DE MEDIO AMBIENTE DEL COLEGIO MÉDICO.

Indicó que el 21 de agosto se generó una crisis y más de 40 pacientes tuvieron problemas, y 24 horas después al medir los gases encontraron tricloroetano -lo mismo que metilcloroformo-, nitrobenceno, tolueno e isobutano. El 23 de agosto se repitió el mismo episodio, con los mismos síntomas y por lo tanto se puede asumir que los compuestos eran los mismos. Fueron 133 los nuevos enfermos. Hubo un tercer episodio el 4 de septiembre, con las mismas características y con 700 personas afectadas.

Señaló que en Chile Oxiquim vende el tricloroetano, pese a ser un gas prohibido de usar, en virtud del Convenio de Montreal, en el que los países desarrollados acordaron terminar con ese compuesto en los años 90, y Chile tenía plazo hasta el 1 de enero del 2015. Sin embargo se estaba usando por alguna empresa.

Consideró grave que la autoridad no informe que gases se encontraron durante los episodios de contaminación. Por ejemplo el metahemoglobinemia debido al efecto del nitrobenceno, que es muy tóxico puede ser causante de daño neurológico, además produce apoptosis neuronal, es decir, muerte neuronal programada.

Respecto del plan de descontaminación sugirió incorporar otros agentes, como arsénico y los distintos solventes orgánicos volátiles.

Indicó que en los episodios de contaminación se debió evacuar a las mujeres embarazadas y a los niños de corta edad, porque el trinitrobenceno, entre otras sustancias, tiene la capacidad de activar el fenómeno del imprinting epigenético, que se relaciona con un cambio en el programa celular que define la calidad y cantidad de receptores de hormonas o de neurotransmisores que las células del individuo van a mantener por toda la vida de la persona. Explicó que las células se van programando a lo largo del desarrollo del embrión y más tarde del feto. En algún momento, algunas células van a definir que formarán parte del epitelio del recubrimiento del estómago, más tarde, algunas de ellas se van a programar para ser las células que producirán el ácido del estómago, y en un período más tardío del desarrollo fetal, se van a programar para definir el número de receptores de la hormona que regula la secreción de ácido por el estómago. Este proceso ocurre en todas las diferentes células del organismo y para todos los receptores de hormonas y neurotransmisores que existen.

Así, en los últimos meses de embarazo o en los primeros años de la vida infantil se realiza una programación en la cual se habrán definido cuántos receptores hormonales van a tener cada uno de los tipos de células. Esta programación ocurre en períodos muy breves de tiempo que se denominan ventanas de vulnerabilidad para distintas células y distintas hormonas.

Si durante el período de vulnerabilidad de algún tipo celular ocurre la presencia de alguna sustancia (contaminante ambiental, fármaco, aditivo de los alimentos o alguna hormona natural en exceso, el programa se altera y las células se programan para tener muchos más receptores o por el contrario muy pocos, lo que va a manifestarse durante toda la vida de la persona.

Si la célula productora de ácido en el estómago se programa para tener demasiado receptores para la hormona que la estimula para secretar ácido, durante toda la vida estas células van a reaccionar en forma desmedida y secretar un exceso de ácido, finalmente se producirá una úlcera, la que se puede perforar, causar una peritonitis y causar la muerte del individuo, muerte que ha sido programada desde antes del nacimiento de dicha persona.

La exposición a contaminantes como el nitrobenceno tiene la capacidad de activar el imprinting epigenético, entonces las células se equivocan y se programan para tener muchos más receptores de hormonas o neurotransmisores y estas alteraciones persistentes de por vida, lo que implica el desarrollo de enfermedades como el cáncer u otras. También las células se pueden programan para no tener los receptores de hormonas o neurotransmisores que debe tener y entonces las personas durante la juventud o a lo largo de la vida, va a desencadenar una diabetes, porque hay muy pocos receptores de insulina.

Por eso es importante combatir la contaminación ambiental con legislaciones que prohíban la incorporación de estos elementos en el uso cotidiano. Se debe prohibir y fiscalizar aquellos procesos que emitan contaminantes peligrosos, y aquellos objetos o sustancias que los contengan y estén en contacto con la sociedad, teniendo especial cuidado con embarazadas y niños, que se encuentran en un período de alta vulnerabilidad.

Finalizó indicando que se debe educar a la comunidad en torno a estos temas, para que adopte las medidas de protección, y, especialmente durante el período fetal y neonatal que son períodos de alta vulnerabilidad. Estas medidas pueden determinar una mejoría sustantiva de las condiciones de salud para las futuras generaciones.

30.-SEÑOR ANDRÉS ROCCATAGLIATA, GERENTE GENERAL DE EMPRESA NACIONAL DEL PETRÓLEO.

Relató que ENAP en la bahía de Quintero, cuenta con un terminal de carga y descarga de crudo que es almacenado en estanques de acopio. Son alrededor de 35 estanques en los cuales se drena el crudo que llega al país con un porcentaje de agua que debe ser decantada y por gravedad se evacua el agua con los riles. Posteriormente esa agua es tratada en los terminales de separación de modo de eliminar el resto de los residuos oleosos y en una piscina se produce la decantación final, y con un emisario esto vuelve al agua.

Sostuvo que en términos de demanda atienden alrededor de 80% o 90% de los combustibles consumidos en el país, específicamente en Santiago, 70% de gasolina de aviones, y 100% de combustible para la zona norte, con una proporción similar en el caso de los combustibles de aviones en la Región Metropolitana.

Se refirió a las operaciones realizadas por ENAP, detallando que existe una boya en la bahía que conecta con los buques a través de un ducto, los que van a parar a los 34 estanques de almacenamiento con los que cuentan. Agregó que después de aproximadamente cuatro días, decanta el crudo y practica el proceso descrito con anterioridad.

Indicó que los estanques requieren un proceso de mantención cada 10 años, de acuerdo a la normativa vigente, por lo tanto, de 34 estanques, se mantienen anualmente de manera constante 3 o 4 en el terminal de Quintero, detallando que el proceso es continuo y de una larga duración, ya que involucra aproximadamente un año, producto del gran tamaño de los estanques, debiendo ser vaciados, limpiados, granallados, además de realizarles una serie de procesos que implican aún más tiempo.

Expresó que un proceso de mantención preventiva de estanques involucra realizar el vaciado del mismo, el retiro de la borra, lo que por efecto de gravedad no puede salir del estanque. Son estanques muy grandes, aproximadamente 35 mil metros cúbicos. Después viene el granallado, es decir, sacar todos los residuos; una mantención mecánica, luego se llenan los estanques con agua de mar para chequear que no haya alguna fuga o filtración, y finalmente está el vaciado del estanque.

Sobre las medidas de seguridad indicó que respecto del proceso de borra de los estanques, el sistema de mantención de los 34 estanques, involucra que sean vaciados cada 10 años del crudo almacenado, lo que genera que en el fondo de los estanques quede una capa espesa de lodos de 15 centímetros, y que producto de la gravedad hace imposible su retiro, razón por la que mediante camiones cisterna, sellados, se extrae la borra y se traslada a un dispositivo API que separa los componentes oleosos del agua para pasar finalmente, a la etapa de decantación, donde se extraen los residuos de hidrocarburos, y a través de un emisario se devuelve el agua al mar, cumpliendo con la normativa que impuesta, en orden a no contaminar la zona marítima de Quintero, en definitiva, sí reconoció la presencia de hidrocarburos pero se encuentran bajo la norma permitida.

Se refirió al sellado de los estanques, la posterior utilización de los riles, el separador API y la piscina, indicando que cuando se ordenó la suspensión del proceso y el sellado de los dos tanques, el agua dejó de correr por los riles.

Explicó que al momento de limpiarse la piscina, se realizó un proceso de extracción de las aguas, las que fueron confinadas en un estanque. Agregó que la evacuación de aguas desde las piscinas, el agua descargada cumple con la norma del sistema de riles. Agregó que ENAP cuenta un laboratorio acreditado por la Superintendencia del Medio Ambiente, la que mensualmente entrega informes de cumplimiento.

Señaló que al momento de efectuarse las fiscalizaciones, se encontraban vaciando los estanques que contenían agua de mar y se cuestionaron los tanques T5109 y el T5104, uno de los estanques estaba vacío porque ya había terminado con

su proceso de mantención y en el otro se estaba evacuando el agua de mar, estaba ya en la última etapa. Además, sostuvo que el año 2018 correspondía realizar la mantención de 4 estanques y se había terminado la mantención de uno, faltando los dos estanques siguientes.

Afirmó que los días 21 y 23 de agosto se produjeron dos eventos de contaminación importantes, los que originaron 300 casos de intoxicación, y en consecuencia, el día 22 de agosto se realizaron labores de fiscalización a ENAP, para posteriormente, el 24 de agosto ordenar la suspensión de labores de mantención, drenaje, uso del separador API y el uso de la piscina.

Manifestó que desde el 24 de agosto, y después en la formulación y acción preventiva realizada por la Superintendencia del Medio Ambiente, se responsabilizó a ENAP como causantes de los episodios de contaminación, asociando directamente los eventos de limpieza del estanque y el uso la piscina como causantes directas del evento de contaminación.

Mencionó que ENAP ha sido fiscalizada en 39 ocasiones por la Superintendencia del Medio Ambiente, la Seremi, la Superintendencia de Electricidad y Combustible y la Policía de Investigaciones.

Expuso que las causas indicadas por la Superintendencia del Medio Ambiente para sustentar la imposición de las medidas preventivas se apoyaron en primer lugar, en la bitácora de Gasmar, donde se señalaba la existencia de un fuerte olor a hidrocarburo, el que aparentemente podría provenir de ENAP, en segundo lugar, en la percepción de olores efectuada por los fiscalizadores de la Superintendencia del Medio Ambiente, pese a que dichos olores eran propios de la operación de hidrocarburos presente al interior de la planta, y en tercer lugar, en la realización de trabajos de mantenimiento que coincidían con las fechas de los eventos de contaminación, sin embargo, el proceso de mantención dura años, por lo tanto, aclaró, que la probabilidad de coincidir los episodios de intoxicación era muy improbable.

Mencionó la implementación de las medidas impuestas por la Superintendencia del Medio Ambiente, además, señaló que desde el 24 de agosto no se está operando en ninguna de las faenas paralizadas, ya que de acuerdo a la resolución dictada, fueron las causantes directas de los episodios de contaminación.

Señaló que los cargos en los que se basa la Superintendencia para indicar a ENAP como responsable directo, es afirmar una falta gravísima que dice relación con el sistema de mantención de los estanques, la que se encontraba fuera de la Resolución de Calificación Ambiental. Dijo que las otras dos faltas eran más bien administrativas, una de ellas es que no se reportó un elemento llamado zinc, que sí estaba informado y la otra es que en 2017 una de las mediciones de los efluentes de la piscina estaba pasada.

Manifestó que posteriormente se dictó un decreto de alerta sanitaria, razón por la que a ENAP se le solicitó formular un plan para enfrentar eventuales episodios de alerta sanitaria, que fue presentado el viernes 24 de agosto, y aprobado el domingo 26 que involucra una reducción del orden de 20% en los componentes de emisiones de gases.

Relató que posteriormente a los eventos del 21 y 23 de agosto, se decretó la paralización de algunas faenas del terminal Quintero, pese a ello han ocurrido otros casos de contaminación.

Agregó que desde el primer día se realizaron estudios técnicos sobre los tres componentes orgánicos volátiles sindicados como causantes de la nube tóxica, sin embargo, no se encontró ningún indicio al respecto, toda vez que dichos componentes no se producen, fabrican, ni utilizan dentro del terminal de Enap. En efecto se contrataron estudios a la Universidad Técnica Federico Santa María y a la Universidad de Santiago de Chile, con el objeto de realizar la medición de los contaminantes emitidos por ENAP en el terminal, y concluyeron la imposibilidad de generarse plumas producto del tratamiento de las aguas riles, en el separador API o en la piscina, menos ser capaz de producir un efecto contaminante como el atribuido a ENAP.

Reconoció la existencia de faltas administrativas, y que en los cargos imputados se encuentra el no cumplimiento de la Resolución de Calificación Ambiental, aludiendo a que dicha situación es de antigua data. Aclaró que de acuerdo a la norma existente, el sistema de mantenimiento de los estanques debe realizarse cada diez años, sin embargo, agregó que los estanques no quedaron contenidos en la resolución de calificación ambiental, siendo la razón por la que se configuró la falta; no obstante, consideró que ello no es tiene relación con el episodio de contaminación ocurrido en la zona de sacrificio.

31.- SEÑOR LUIS MANRÍQUEZ BALMACEDA, GERENTE DE OPERACIONES DE LA EMPRESA NACIONAL DEL PETRÓLEO.

Aclaró que las borras se retiran en el inicio del proceso de mantención, que dura un año. Y que uno de los tanques fiscalizados se encontraba seco, es decir, no mantenía borra, mientras que el otro tanque se encontraba en proceso de retirado del agua de la prueba hermética. Explicó que es imposible que las borras sean retiradas en camiones producto de su densidad, por lo tanto, se retiran de manera mecánica, con pala y carretillas; actividad que fue realizada hace más de un año, entre marzo y abril.

Expresó que lo que existió fue una confusión de terminología, y aclaró que las labores realizadas correspondían al retiro de agua del proceso de prueba hermética de los tanques, momento en que se realizó la fiscalización.

32.- SEÑOR GABRIEL MÉNDEZ, REPRESENTANTE LEGAL DE ENAP.

Indicó la disposición de Enap a compartir los antecedentes de las operaciones de carga de crudo iraní en las instalaciones de ENAP, que han podido recopilar durante las investigaciones en curso, teniendo presente que eso también es parte de investigaciones administrativas que realiza la Superintendencia del Medio Ambiente y de una investigación enmarcada en una causa que lleva adelante el Ministerio Público, a través de la Fiscalía Regional del Biobío.

En términos de una cronología de hechos, durante el mes de julio y antes de que la nave Monte Toledo arribara a la bahía de Concepción, dijo que se informó que el crudo transportaba una alta concentración de ácido sulfhídrico. En condiciones normales en términos de operación, el crudo iraní es un crudo que se negocia y se distribuye abiertamente a lo largo del mundo, pero en condiciones superiores en

términos de sulfhídrico a las que regularmente se recibían en esa época en embarques en la misma bahía de Concepción para la ENAP.

La nave arribó a la bahía de Concepción el 14 de julio de 2018 en un buque conocido como el Monte Toledo, dado que tenía su capacidad de carga completa y, por tanto, no podía ingresar a la Villa San Vicente, se dispuso la realización de una maniobra de alije, de trasvasije, de la mitad del crudo a una nave menor, Cabo Victoria era su nombre, la que transportaría parte de ese crudo a la comuna de Quintero.

Hizo énfasis en que, frente a la información de un importante contenido de ácido sulfhídrico en ese crudo, se ejecutaron y se expusieron las medidas adecuadas y necesarias en términos de realizar una operación de recepción del producto lo más segura posible.

Explicó que primero es generar un análisis sistemático de riesgo, documentos que se presentan ante la autoridad naval y marítima, donde se establecen todas las condiciones en virtud de las cuales se debe hacer la operación tanto de alije, de trasvasije de crudo de una embarcación a otra, como de descarga del crudo en los puertos y en los muelles donde será recibido.

Expresó que, lo que se hace antes de realizar cualquier actividad es presentar esos dos análisis sistemáticos de riesgo -uno para las maniobras de alije y el otro para la descarga- a la autoridad marítima para que autorice las condiciones en virtud de las cuales se deben llevar a cabo esas operaciones. Al mismo tiempo, como es usual en este tipo de operaciones, se buscó y contrató a la empresa internacional más importante en este rubro -la compañía Baker Hughes empresa americana filial de General Electric (GE)- para que se hiciese cargo de todo el proceso de tratamiento y asegurar las condiciones para realizar el alije y la descarga del crudo, dado el contenido de ácido sulfhídrico que tenía. Lo que se le encarga a ellos es un proceso de tratamiento que neutraliza el sulfhídrico antes de que se refine en las refinerías de la ENAP. Para ello, se utilizó un compuesto, un secuestrante de ácido sulfhídrico, la que opera y se encarga de esa operación la empresa Baker Hughes-, el cual fue fabricado y suministrado por Oxiquim, quien lo produjo en su planta de Coronel.

Ahora bien, el secuestrante de ácido sulfhídrico se introduce en tierra en un circuito cerrado. Todas estas operaciones, para que sean seguras, se realizan a través de circuitos cerrados que no generen emanaciones.

Entonces, en Talcahuano, una vez que la autoridad naval revisó esos análisis sistemáticos de riesgo y autorizó las operaciones de alije y descarga con las condiciones que allí fueron establecidas, se procedió a una maniobra de alije los días 3 y 4 de agosto del 2018, en la Bahía Concepción.

Indicó que durante la maniobra de alije, personal de la Armada inspeccionó el buque Monte Toledo. Explicó que se produce en la parte de la operación que se considera más sensible en relación con la fugas de potenciales gases, la desconexión que existe entre los flexibles que unen los distintos barcos. En ese momento se encontraba en cubierta del buque Monte Toledo personal de la autoridad marítima, personal naval que supervisa la maniobra, que establecen mediciones y que luego de que se realiza la operación emite un certificado en la Dirección General del Territorio Marítimo y Marina Mercante de Chile (Directemar) estableciendo que la concentración de sulfhídrico durante la maniobra y al término de

la misma era de cero y que se verificaron las condiciones normales de mediciones de gases y faenas de alije.

Durante esta operación no se produjeron afectaciones a la salud ni síntomas de intoxicación en el personal de la ENAP que participó en ella, ni en el personal de los buques Monte Toledo o Cabo Victoria y tampoco en el personal de la Armada.

Luego, la siguiente fase, fue el desembarco de descarga de crudo que se realizó en la bahía de San Vicente el 5 de agosto. Ese día se inicia el proceso de descarga del crudo y el 7 de agosto en la bahía de San Vicente en Talcahuano se termina el proceso de descarga de la parte que quedaba en el buque Monte Toledo. La descarga también se realiza en un circuito cerrado que impide la emanación de gases.

Hizo presente que, San Vicente, que es el terminal de ENAP en Talcahuano, no tiene tanques receptores de crudo sino que son tuberías directas a la refinería.

Insistió en que todo lo relacionado con la verificación y proceso de tratamiento del sulfhídrico a través de este secuestrante fue realizado por la empresa Baker Hughes, tal como se había establecido, según las condiciones contenidas en el análisis de riesgo para la operación.

Luego de que se inyecta el secuestrante, esta operación a través de Baker Hughes, se hacen mediciones, por cierto, donde el nivel de sulfhídrico que aparece son, en condiciones normales, inofensivas para la salud humana.

Como tercera operación se da la descarga de crudo e inyección de secuestrante en la bahía de Quintero.

Sostuvo que en la bahía de Quintero no se hizo ningún alije ni un proceso de trasvasije entre un buque u otro. Las maniobras de descarga del crudo se realizan entre los días 8 y 9 de agosto desde el buque Cabo Victoria al terminal que tiene ENAP en Quintero. Se utiliza en la misma documentación las mismas medidas establecidas en el análisis sistemático de riesgos que se utilizan en Biobío, con la autorización, por cierto, de la autoridad naval de la zona.

Agregó que el procedimiento de uso e inyección del secuestrante para asegurar que hayan condiciones de sulfhídrico normales en ese crudo al llegar al terminal y a la refinería son también ejecutadas por personal Baker Hughes. Se utiliza el mismo producto empleado en la VIII región, fabricado por Oxiquim.

Prosiguió diciendo que la inyección de secuestrante se hace en un punto de tierra en un circuito cerrado en una línea de descarga. Luego eso, en el caso de Quintero, el crudo se deposita en los estanques; en tres estanques, el 5102, el 5108 y el 5111, del terminal de Quintero. Esos estanques no estaban en proceso de mantención. Mencionó esto porque es importante señalar que las medidas profesionales adoptadas para la Superintendencia, y después el proceso de levantamiento de cargos de la Superintendencia, hacen referencia a otros dos estanques distintos a los que mencionó, los que sí estaban en proceso de mantención.

Las mediciones de sulfhídrico, luego de aplicado el secuestrante, también arrojan valores normales inofensivos para la salud, semejante a los valores arrojados en los casos de Biobío.

En el proceso de descarga del crudo e inyección de secuestrante, el 8 y el 9 de agosto, no se reportaron malos olores ni incidentes que hayan afectado a trabajadores de ENAP ni de Baker Hughes, ni tampoco se reportan incidentes en Quintero ni Puchuncaví durante esos dos días.

33.- SEÑOR JUAN DOMINGO ACOSTA, ASESOR JURIDICO ENAP.

Explicó que respecto de la investigación seguida ante el Ministerio Público, la Fiscal a cargo ha requerido antecedentes a la ENAP y sostuvo que como empresa han colaborado con la investigación en todo lo solicitado.

Precisó que el ácido sulfhídrico lo contienen prácticamente todos los crudos. Es normal que los crudos tengan mayores o menores concentraciones de sulfhídricos. Aseveró que el que provenía de Irán tenía una concentración especialmente alta, que no significa que sea un crudo que no se pueda utilizar, sino que hay que neutralizarlo. Para este efecto y como la ENAP no es experta se contrató a Baker Hughes, que es líder mundial.

Agregó que esta empresa decidió cuál era el producto que había que incorporar y se lo encargó a Oxiquim, siendo los resultados exitosos porque la reducción del sulfhídrico llegó a niveles que varían entre 2 y 10 ppm. El nivel de tolerancia del sulfhídrico es de 100.

El sulfhídrico es un veneno; pero con los resguardos que se tomaron no se puede pensar que hubo una emanación de sulfhídricos en la maniobra de alije del día 4, o después, en la descarga de crudo. De ahí que se concluya que si quienes estuvieron presentes no tuvieron síntomas de intoxicación menos la población que estaba lejos del lugar de la maniobra.

Aseguró que todas las condiciones que se utilizaron para esto fueron de la mayor seguridad. Se desarrollaron en un ambiente cerrado, en un ambiente confinado, y por ello aseguró que no hubo emanaciones. Agregó que este procedimiento fue monitoreado, no solo por la Armada, sino también por la ENAP. Hubo cuatro monitoreos en línea y una empresa especializada, distinta a la Armada, contratada para estos efectos, que emitió todos sus informes y hora tras hora reportó los resultados que se iban obteniendo.

Respecto de la maniobra de descarga, los resultados fueron exactamente los mismos. Evidentemente, ahí no intervino la autoridad marítima, porque no era una maniobra que necesitara una supervisión directa de ella. Los resultados fueron también en el mismo sentido: variaciones entre 2 y 10 ppm de sulfhídrico. O sea, cantidades son inocuas.

Finalizó indicando que quienes trabajan con crudo directamente, tienen un solo detector: la de gases de sulfhídrico, y no se activó durante las maniobras.

34.- SEÑOR ANTONIO BACIGALUPO, GERENTE GENERAL DE GNL.

Relató que GNL Quintero cuenta con un terminal en la bahía que opera desde el año 2009 con estándares de clase mundial; el que recibe buques con gas natural licuado enfriado a temperatura de -160 grados, con el objeto de llegar a estado líquido, el que posteriormente se descarga y almacena en el terminal, para finalmente ser regasificado a través de un proceso de sistema cerrado de intercambio de calor, el que prácticamente, no genera emisiones de ningún tipo a la atmósfera, razón por la que afirmó que el sistema es cerrado con un combustible limpio.

Sostuvo que el terminal cuenta con un importante rol en la matriz energética de Chile, la que entrega 100% de gas natural consumido en la Quinta Región, en la Región Metropolitana y en la Sexta Región. Además, indicó que a través de camiones se traslada el gas natural licuado a clientes -de Puerto Montt a La Serena-, y se abastece a clientes residenciales, comerciales, industriales, de generación eléctrica y transporte.

Explicó que todas las instalaciones y procesos del terminal han sido sometidos a un sistema de evaluación de impacto ambiental, los que cuentan con resoluciones de calificación ambiental, las que han sido cumplidas de manera estricta desde el inicio de las operaciones. Enfatizó que GNL ha operado de manera limpia y responsable en la comunidad de Quintero, bajo la lógica de la sostenibilidad.

35.- SEÑOR ALFONSO SALINAS, GERENTE GENERAL DE SOSTENIBILIDAD DE GNL.

Explicó que el gas natural básicamente es un hidrocarburo llamado metano, el que es más liviano que el aire, cuya función principal es ser utilizado como combustible, salvo que se queme. Relacionó lo anterior, indicando que no existe fuga en el terminal de GNL, agregando que al ser el metano más liviano que el aire, -al igual que el esmog-, éste sube, siendo capaz de llegar a una población.

Añadió que el gas natural no es tóxico, y para llegar a serlo se tendría que contravenir todas las características físico-químicas del producto para que saliera, no se quemara, bajara, se oliera, intoxicara, sin embargo, no presenta ninguna de estas características. El gas natural que es traído en barco se encuentra en estado líquido, ya que al ser como agua pueden estar en estado de vapor, sobre 100°C, o de hielo en caso de enfriarse. Agregó que el metano (CH_4) a -160°C, pasa de ser un gas a un líquido, reduciendo su volumen 600 veces y que para ello se utilizan tuberías que cuentan una importante aislación para mantener dicha temperatura. Indicó que de advertirse alguna fuga ésta se calentaría y evaporaría dentro del terminal, lo que contravendría el proceso.

Además los barcos traen gas líquido en termos herméticos que no pueden tener “venteos”, y al momento de atracar el barco, donde un práctico se sube con un *notebook* y ve de manera satelital al barco con la precisión de dos centímetros, para posteriormente, atracar el barco al terminal y adosarlo a los brazos de descarga de manera hermética, no pudiendo fugarse nada de GNL, el que se encuentra frío y asilado de la temperatura ambiente, ya que está sometido a -160°C, los que luego son depositados en dos estanques por razones de seguridad, posando sobre 260 aisladores sísmicos.

Sostuvo que GNL no agrega ningún tipo de gas, y que son las empresas que comercializan en la ciudad quienes agregan gas odorante para ser percibido, recalcando que en el terminal no se ocupa mercaptano.

Sobre las estaciones de monitoreo y la falla, indicó que es el mismo Estado el que estableció que las empresas debían contratar a especialistas para efectuar los monitoreos. Aclaró que no se contrata a cualquier empresa, sino que se a un laboratorio independiente, que cuente con certificación, como ocurre con la empresa SGS que cuenta con más de 2.400 oficinas en el mundo, la que además es totalmente autónoma. Agregó que la política pública que se siguió en la legislación ambiental chilena fue que las empresas, que en el fondo potencialmente contaminan, sean las que paguen, pese a ello, se tiene que contratar a empresas certificadas y auditadas por la autoridad, por lo tanto, en el caso de monitoreo de calidad del aire, este se realiza a través de un equipo operado y situado en el centro de Quintero por la empresa externa SGS.

Afirmó que los equipos son mantenidos de acuerdo a protocolos estrictos, siendo auditados por parte de la Superintendencia de manera periódica.

Expresó que el problema histórico de contaminación de la bahía no se restringe a un problema de calidad del aire, sino que además considera temas de suelo, agua, etcétera, sin embargo, indicó que no tiene sentido preguntar si una empresa determinada tiene o no la capacidad física de producir emanaciones. Sostuvo que si bien todas las empresas dicen que cumplen con las normativas, es importante contar con una exigencia a nivel técnico que permita poner a prueba ello.

Evidenció que existen ciertos eventos de combustión asociados a los problemas de contaminación atmosférica, particularmente, con el dióxido de azufre, y otros eventos relacionados con compuestos orgánicos volátiles, siendo necesario otro tipo de equipamiento, como termómetros, razón por la que se realizó el estudio Asiva.

Relató que para tener garantías, se decidió contratar a un especialista independiente, doctor en Química por la Universidad de Chile y posdoctorado por UCLA, quien determinó las empresas que podrían llegar a tener algún potencial en alguna situación operacional particular, y el tipo de contaminantes que podrían estar presentes, además, recomendó el equipamiento de monitoreo necesario para pesquisar de manera analítica.

Sostuvo que de manera voluntaria, se entregaron todos los parámetros en línea, para que la autoridad pudiera verlos de forma inmediata, pese a no estar en la resolución de calificación ambiental. Añadió que sería necesario otro tipo de equipamiento para poder especificar los hidrocarburos no metálicos, y de esa manera tener certidumbre sobre lo que está produciendo este tipo de casos.

Reconoció que si bien el equipo presentó fallas, desde el momento en que se avisó dicha situación, se reparó en un día, por lo tanto, los días posteriores, donde se evidenció los casos de gente intoxicada, se realizaron las mediciones pertinentes.

Respecto a las fiscalizaciones y sanciones indicó que aumentaron su número desde el momento en que ocurrieron los eventos de intoxicación, toda vez que se han realizado 14 fiscalizaciones y 15 requerimientos de información. Explicó que normalmente se realizaban solo un par de fiscalizaciones ambientales, de la Superintendencia de Electricidad y Combustibles (SEC) y de otras autoridades.

Añadió que las normas existentes en Chile son laxas y que hay parámetros donde no existen normativas.

36.- SEÑOR EDMUNDO PUENTES RUIZ, GERENTE GENERAL DE OXIQUIM.

Relató que el terminal marítimo de Oxiquim de Quintero se construyó a principios de los 80, cuando en Chile aun no existía un terminal marítimo para la importación de materias primas petroquímicas. En 1994 se construyó el terminal marítimo actual, en el mismo lugar donde estaba el original, cuyo diseño se realizó de acuerdo a los estándares vigentes internacionalmente y en conformidad con las normas chilenas aplicables. Explicó que los diseños se hacen de acuerdo con las normas API, *American Petroleum Institute*; de la NFPA, *National Fire Protection Association*, la que regula todo lo relacionado con el manejo de productos inflamables, y otras normas aplicables.

Sostuvo que el terminal marítimo es una instalación destinada únicamente a dar servicio de recepción, almacenamiento y despacho de graneles líquidos, principalmente gas licuado de petróleo, además de combustibles limpios y productos químicos que la manufactura nacional requiere como tal y que Oxiquim contaba con todos los elementos necesarios para asegurar la inexistencia de toda mezcla accidental de diferentes productos, como así también, de contaminaciones cruzadas.

Señaló que todos los sistemas de gestión, mencionados con anterioridad, se encuentran acreditados con certificados vigentes emitidos por los organismos certificadores con validez internacional.

Asimismo descartó que al interior del terminal de Oxiquim se realizaran procesos de fabricación, mezclas, ni envasado, agregando que la seguridad de las operaciones se gestiona con el apoyo de los sistemas de gestión internacional: CDI-T, *Chemical Distribution Institute-Terminals* (norma de origen europeo); el *International Ship and Port Security Codek* (norma de origen norteamericano) y el programa Conducta Responsable que acuñó la industria química canadiense, la que actualmente se ha expandido por los principales países del mundo.

Reafirmó que Oxiquim no ha generado los *peaks* de contaminación, como se ha constado en las 43 inspecciones realizadas al terminal desde los días 22 de agosto hasta la fecha.

Manifestó que a GNL le han realizado 18 inspecciones por parte de la Superintendencia de Medio Ambiente; 18 por la Seremi de Salud; 3 de la Secretaría de Electricidad y Combustibles; 1 por el departamento de Medio Ambiente de la Municipalidad de Quintero, y 3 de la brigada de delitos medioambientales de la Policía de Investigaciones de Chile. Agregó que además se han instruido dos sumarios en contra de GNL

El primer sumario fue por almacenar xileno producto clase 3, inflamable, en el estanque 306. Destacó que el 5 de enero de 2017, Oxiquim le solicitó a la SEREMI de Salud de Viña del Mar la modificación de la Resolución Nº 806, de 2015 para utilizar diversos estanques como multiproducto, entre ellos, el estanque 306 para uso en clase 3, 6, 8 y 9. Explicó que un estanque puede ser utilizado como multiproducto, lo que significa que en cada oportunidad puede almacenar productos distintos de aquellos para los que fue diseñado. Indicó que una vez almacenado un

producto, el estanque es vaciado, limpiado para almacenar otro producto distinto de entre aquellos para los cuales está autorizado.

Respecto a las noticias difundidas acerca de la detección de tres contaminantes en el monitoreo del aire, sostuvo que ello era erróneo y que el metilcloroformo, no era importado y que no se registran importaciones al país de acuerdo con las estadísticas de importación de Aduanas.

Consultado sobre los trabajadores del terminal de Oxiquim afectados, indicó que no hubo trabajadores propios que hayan acusado síntomas de malestar asociados a la contaminación, evidenciando que solo manifestaron malestares dos estudiantes en práctica y tres trabajadores de contratistas. Los primeros fueron trasladados al hospital de Quintero, acompañados por la encargada de prevención de riesgos del terminal, lugar en donde esperaban para ser atendidos, momentos en los que llegaron sus padres y declararon sentirse mejor, sin embargo, producto de la larga espera para ser atendidos, sus familiares decidieron trasladarlos a sus hogares. Respecto de los segundos, preciso que todos la prevencionista y los dos guardias de seguridad de la empresa *Guard Service,* decidieron irse a su casa porque se encontraba mejor, aun cuando se le indicó a loa contratista que los derivara a a la mutualidad.

Preguntado sobre la aprobación por la Comisión Regional de Uso del Borde Costero, de la concesión marítima que permite a la empresa la construcción y operación de un muelle multipropósito, expresó que Oxiquim tiene concesiones marítimas que están en uso y otra como proyecto. El proyecto de terminal portuario multipropósito duró nueve años su tramitación y que cuando se trató dicho proyecto en la Comisión Regional de Uso de Borde Costero -hace unos siete u ocho años- y se aprobó con votación en contra y a favor. Indicó que hace aproximadamente cuatro años se inició la tramitación de una ampliación del objeto de la concesión de este proyecto, con el objeto de incluir cargas de concentrado de cobre; descarga de granos; de clínker, para la industria de cemento, y carga de graneles líquidos, por eso se llama múltiple multipropósito. Indicó que el proyecto se votó antes de otorgar la ampliación de la concesión y que el Subsecretario de las Fuerzas Armadas lo mandó por segunda vez en consulta a la Comisión Regional de Uso de Borde Costero y que posteriormente la votación dio un resultado de 18 votos a favor y 8 o 9 votos en contra, sin la presencia de los alcaldes de las comunas de Puchuncaví y Quintero.

Agregó que el carbón era parte original del material, pero en la actualidad se ha descartado ya que su finalidad se sustentaba en abastecer un proyecto de Codelco, y en el caso del percolado manifestó que está totalmente descartado, ya que no es parte de la ampliación del objeto.

Declaró que la empresa ha recibido 43 fiscalizaciones, teniendo gran parte de dichas fiscalizaciones una duración mínima de 5 horas, llegando incluso a las 10 horas, tiempo en el que el fiscal levantaba todos los detalles e información posible.

Consultado sobre el acta de fiscalización en que se destaca que Oxiquim “se encuentra almacenando sustancias peligrosas en estanques no aptos para ello”, respondió que el estanque 306, donde se almacenaba xileno, -producto inflamable-, corresponde a un estanque habilitado para almacenar productos técnicamente inflamables, encontrándose acreditado por un certificado de una firma certificadora independiente. Además, explicó que los permisos se encontraban en proceso, es decir, no se encontraban denegados, pero tampoco estaban aceptados. Agregó que

la SEREMI de Salud tomó una medida precautoria, instruyendo no mover el producto hasta que se resolviera el sumario, estanque que se encuentra sin movimiento desde el momento en que se levantó dicha decisión, lo que se ha podido acreditar tras las fiscalizaciones efectuadas

37.- SEÑOR JAVIER GIORGIO, VICEPRESIDENTE DE OPERACIONES DE AES GENER

Explicó que AES Gener es una compañía eléctrica que tiene como visión seguir creciendo e invirtiendo en Chile en activos renovables, enfocando las inversiones en energía solar, viento, baterías y desalación. Agregó que la empresa se ha comprometido a no construir más plantas a carbón en Chile, y así en los últimos cuatro años es la compañía que genera más energía eléctrica, con una participación en el mercado de 27%.

Precisó que el complejo Ventanas está compuesto por 4 unidades generadoras de electricidad a partir de la combustión de carbón con distintas fechas de entrada en operación. Evidenció que la más antigua es Ventanas 1, que data es de 1964; Ventanas 2, de 1977; Ventanas 3, de 2010, y Ventanas 4, de 2013. Añadió que la empresa cuenta con una capacidad instalada de 862 MegaVatios, lo que se traduce en una generación de energía equivalente al 8% del total introducido en el país. Y que en las dos últimas unidades se han invertido cerca de mil millones de dólares, trabajando 225 personas directamente por AES Gener y 557 colaboradores externos, de los cuales 45% habita en la zona.

Sostuvo que las instalaciones dentro del complejo industrial se encuentran sometidas a una fuerte regulación medioambiental; además de Resoluciones de Impacto Ambiental, plan de descontaminación vigente, siendo alcanzados por la norma de emisiones a termoeléctricas, del DS N° 13, del 2011.

Explicó que las normas que regulan a AES Gener lo hacen desde un punto de vista ambiental y de gran exigencia, existiendo límites de emisión, lo que motivó realizar inversiones importantes. Expuso que en Chile se ha invertido 437 millones de dólares, de los cuales 115 fueron aplicados en equipos de abatimiento para las unidades 1 y 2, mientras que las unidades 3 y 4 desde su instalación cuentan con los equipos necesarios para cumplir la norma. Agregando que solo en Ventanas se ha invertido 250 millones de dólares en distintas mejoras ambientales, de los cuales 115 se encuentran ocupados directamente en la instalación de equipos de abatimiento.

Expuso que las distintas normas fueron incrementando sus niveles de exigencia, ejemplificando lo anterior, con las Resoluciones de Calificación Ambiental y el decreto N° 252, los que anteriormente eran sumamente laxas, mientras que en la actualidad el Decreto Supremo N° 13 limita el material particulado (MP).

No obstante, manifestó que a pesar de un importante incremento en la energía generada, producto de la adición de las unidades 3 y 4, el complejo en total ha disminuido significativamente las emisiones, las que se encuentran muy por debajo de lo exigido en la norma aplicable, producto de la inversión realizada en equipos de abatimiento. Precisó que lo mismo sucede respecto al SO2, toda vez que la norma de emisión se ha vuelto cada vez más exigente, pese a haber adicionado las unidades 3 y 4, se advierte un aumento en la generación de energía, pero con un menor nivel de emisión que está por debajo del límite impuesto por la normativa actual, al igual que en el caso de NOx, encontrándonos por debajo de la norma.

Advirtió que las inversiones redujeron la emisión de los tres materiales lanzados a la atmósfera, los que corresponden a: SO2, experimentando una baja de emisión de un 32%; NOx 37% y Material Particulado (MP) de 36%.

Señaló que eventos de intoxicación se pueden producir por *peaks* de emisión y por condiciones atmosféricas desfavorables, como se evidenciaron en el mes de agosto, con condiciones de ventilación irregulares y de regulares a buenos.

Manifestó que las emisiones del complejo Ventanas en SO2, NOx y MP son estables en el tiempo. Indicó que AES Gener tratando de colaborar para esclarecer los hechos ocurridos, ha instalado una sala de monitoreo para controlar las emisiones, y mantener una capacidad de reacción frente a las alzas.

Expuso que AES Gener traspasó el control de la red de calidad al Ministerio del Medio Ambiente, suspendiendo de manera temporal la producción en la planta Ventanas 1 ante la dictación del decreto de alerta sanitaria. Expresó que se entregó el plan operacional, que fue aprobado, en el cual se programa disminuir en un 10% las emisiones de SO2, cada vez que se genere una contingencia ambiental por una condición de mala calidad del aire y una condición meteorológica adversa.

Indicó que además, contribuyen de manera proactiva a la mejora de los sistemas de monitoreo de calidad del aire, trabajando con SOFOFA, y el instituto VTT de Finlandia, con la finalidad de disponer de una red de monitoreo más moderna y acorde a las necesidades de la zona.

Explicó que en lo que va del año han sido objeto de 31 fiscalizaciones, 29 de ellas asociadas a los eventos en Quintero y Puchuncaví, no siendo sometidos hasta la fecha a ningún sumario y ningún trabajador de la empresa ha resultado afectado por los episodios de intoxicación.

Advirtió que de no otorgárseles los permisos no harán la inversión en una nueva instalación para transferir los productos de la solicitud. Sin embargo, indicó que se inhibiría la competencia en la zona y se inhibe la introducción de nuevas tecnologías, porque un nuevo proyecto parte con tecnologías actuales. Muchas de las instalaciones de la zona son bastante antiguas, y en ese sentido el proyecto representa un beneficio para la autoridad, para la comunidad y para el país.

38.- SEÑOR MILTON ROSALES, GERENTE DE MEDIO AMBIENTE DE AES GENER.

Indicó que los datos sobre los cuales se basa la elaboración de estos planes son muy deficientes y erróneos porque se trata de información antigua, obsoleta y que no representaba las reales emisiones o las autorizaciones de las unidades de AES Gener, que eran públicas y que podían haber sido recopiladas también por la autoridad.

Sobre la posibilidad de reducir en 10% las emisiones de SO2 en forma parmente, sostuvo que ello no era posible por cuanto puede exigirle al equipo de abatimiento trabajar con mayores exigencias, adicionando mayor cal, sin embargo, ello no puede realizarse de forma continua, ya que dañaría el equipo desulfurizador, razón por la que se han ofrecido dichas reducciones, las que se van a instaurar cada vez que exista una contingencia ambiental.

Relató que durante el último período, se realizaron alrededor de 30 fiscalizaciones, sin embargo, en periodo normal se realizan entre 6 a 10 fiscalizaciones al año, ya sea por la propia Superintendencia o por distintos servicios mandatados en nombre de la Superintendencia, como salud o la Superintendencia de Electricidad y Combustibles, los que habitualmente estaban vinculados a las Resoluciones de Calificación Ambiental.

39.- SEÑOR JOSÉ SANHUEZA REYES, GERENTE GENERAL CODELCO DIVISIÓN VENTANAS.

Explicó que Codelco División Ventanas es un complejo industrial construido en 1964 por Enami, y que en ese entonces comprendía solo dos empresas, Chilectra y Codelco División Ventanas, mientras que en la actualidad existen más de 14 industrias.

Manifestó que existe una red de monitoreo ambiental, que opera desde 2012, la que se encuentra abierta las 24 horas del día y que Codelco División Ventanas cuenta con siete monitores que miden la calidad del aire del polo industrial de todos los emisores de CO_2, con un perímetro de monitoreo de alrededor de dos kilómetros. Expuso que anteriormente Codelco era administrada por una empresa independiente, pasando su administración al Estado a partir del 9 de septiembre de 2018.

Destacó que siendo una división que no se caracteriza por su rentabilidad, es la primera fundición estatal que cumple el DS 28, desde el 12 de diciembre de 2016, que regula capturas de CO_2 y de arsénico con niveles mínimos de 95%, además de emisiones y además regula en forma continua las emisiones de la planta de ácido, la que está conectada directamente con Salud y Medio Ambiente.

Explicó que si bien la nueva normativa establece un máximo de arsénico de 40 toneladas al año, Codelco genera emisiones inferiores a 40 y manifestó que producto de la inversión efectuada se logró reducir en un 30% las emisiones de dióxido de azufre. Agregó que cuando partió el proyecto el 2011, el año anterior habían emitido aproximadamente 15.600 toneladas de SO2. El año 2017 bajó a 10.500 toneladas de SO2, o sea se redujo 32 por ciento lo que no estaban emitiendo por efecto de los proyectos.

Agregó que la inversión anual, en los últimos 5 o 6 años ha sido de un promedio de 25 a 30 millones de dólares, culminando el año 2016 con una cifra récord de más de 40 millones para la implementación de 12 proyectos.

Expuso que Codelco División Ventanas cuenta con una norma de 95%, superándola y situándose en un 95,7%, reduciendo las emisiones de CO_2. En 2015 se mantenían emisiones del orden de 14.000 toneladas, existiendo periodos en que las emisiones superaban las 20.000 toneladas, con valores sustancialmente mayores.

Manifestó que una vez al mes se deben entregar todos los balances del complejo industrial, informando a la Superintendencia los niveles de emisión de material particulado, de CO_2, de arsénico, etc., es decir, de todo los elementos que aparecen normados en el decreto.

40.- SEÑOR JORGE LAGOS RODRÍGUEZ, GERENTE DE SUSTENTABILIDAD Y RELATIVOS INSTITUCIONALES DE CODELCO DIVISIÓN VENTANAS.

Señaló que la concentración de dióxido de azufre (SO2) del día 21 de agosto fue menor a 100 microgramos por metro cúbico normal y el 23 de agosto fue del orden de los 50 microgramos, es decir, ambas concentraciones son bajísimas.

Agregó que efectivamente hubo un peak cercano a los 500 microgramos 27 horas antes de que se generara la intoxicación de los primeros niños intoxicados, sin embardo descartó que este hecho tenga relación con el peak porque cuando hay intoxicación por gases, los efectos son instantáneos y no 27 horas después.

Señaló que en un monitoreo realizado el 24 de septiembre se evidenció condiciones muy bajas de concentración, en el orden de los 100 microgramos por metro cúbico, identificándose a las 11.00 50 microgramos por metro cúbico normal.

Explicó que respecto del peak, que Codelco División Ventanas es emisora de material particulado y de CO2, sin embargo se cumplen con todas las normas, e incluso las inexistentes.

Indicó que de acuerdo a lo indicado por la Agencia de Protección del Medio Ambiente Americana, los efectos del SO2 (dióxido de azufre) se manifiestan con irritación de las vías respiratorias y afectación leve en los ojos, descotándose los síntomas de nauseas, vómitos, cefaleas y parestesia, como ocurrió los días de intoxicación masiva en el sector, sin embargo relacionó los episodios de contaminación con hidrocarburo, no obstante, manifestó estar tranquilos porque han realizado las inversiones necesarias para cumplir con las normas. Incluso detalló que luego de las intoxicaciones han sido fiscalizado por la Superintendencia y por el Servicio de Salud 45 veces sin encontrar ninguna deficiencia.

Manifestó que Codelco División Ventanas ha realizado todos los esfuerzos posibles para cumplir con la norma de calidad en las zonas en la que operan, especialmente las normas de emisión del decreto N° 28 son cumplidas a cabalidad, e incluso excediendo lo solicitado y que siempre ha existido disposición para implementar y cumplir con las normas existentes, respetándolas, lo que se manifiesta en un porcentaje de captura superior a lo solicitado por la norma.

Reconoció la existencia de instalaciones al interior de Codelco División Ventanas que no cuentan con Resolución de Calificación Ambiental, lo que se explica al ser un complejo del año 1964, mientras que las RCA comenzaron en el año 1997, razón por la que todos los proyectos posteriores a 1997 cuentan con RCA.

Señaló que en la zona existen diez resoluciones de calificación ambiental, las que son fiscalizadas con habitualidad, y que corresponden a proyectos relacionados con la norma de emisión. Preguntado sobre someterse a un estudio de impacto ambiental, indicó que el Estudio de Impacto Ambiental y el Sistema de Evaluación de Impacto Ambiental, por definición, son herramientas preventivas, se realizan análisis y estudios antes de ejecutar un proyecto, por lo tanto, manifestó que hacer un estudio de impacto ambiental después de un proyecto ejecutado tendría que recibir otra denominación.

Comentó que más que dar una solución como empresa, es necesaria una política de Estado, más que con indicaciones que pueda efectuar Codelco División Ventanas.

Explicó que con los planes de descontaminación, se le exige a las empresas bajar sus niveles de emisión, teniendo como única opción Codelco en la actualidad, disminuir la producción y todo lo que ello significa. Sin embargo las normas de calidad y de emisión son a nivel país.

Sostuvo que la norma actual de calidad regula a todo Chile, no solo a Codelco-Ventanas, agregando, que de evaluar la situación, es posible advertir que falta una norma de calidad, razón por la que se habla de exposición de promedios horarios.

Finalizó precisando que hay una norma anual y una diaria que están bajo un estándar, por ello es obvio que deben mejorarse y agregar una norma horaria que permita ver cómo se comporta y los efectos posibles. Comparo el proceso con dar el examen de conducir y comprarse de inmediato un Ferrari.

41.- SEÑOR GERMÁN OYOLA, EXJEFE DE DIVISIÓN DE CALIDAD DEL AIRE Y CAMBIO CLIMÁTICO DEL MINISTERIO DEL MEDIO AMBIENTE.

Relató que asumió como jefe de la División de Calidad del Aire en septiembre de 2015 y renunció el 30 de junio de 2017 al Ministerio, sin embargo por razones médicas estuvo fuera desde el 20 de marzo y el día que volvió renunció.

Sobre las funciones que cumplió en la división de calidad del aire indicó que tenía un cargo de asesor técnico de la jefatura en las distintas materias que eran competencia de la división. Además, señaló haber estado a cargo del desarrollo de los planes, de las normas, la operación de las redes de monitoreo y el departamento de cambio climático.

Señaló que el gobierno anterior ingresó 14 planes de descontaminación para las diversas regiones y para revisión: de los cuales, 10 estaban vigentes y 4 rechazados (entre ellos, el correspondiente a la zona de Concón, Quintero y Puchuncaví).

Respecto del plan de descontaminación sostuvo que fue aprobado por el Consejo de Ministros en diciembre de 2016, e ingresado a la Contraloría el 28 de marzo de 2017, advirtió que durante ese período, no era el jefe de la división, pero continuaba prestando funciones en el Ministerio.

Indicó que, la Contraloría envió observaciones al Ministerio en julio de 2017, cuando ya no estaba en el Ministerio, sin embargo, tuvo conocimiento que se referían al inventario de emisiones y a la regulación de calderas.

Hizo presente lo complejo de la elaboración del plan, asociado al contexto normativo: implementar normas de emisiones para fundiciones y termoeléctricas; el desarrollo de una normativa de calidad del aire para dióxido de azufre y para la emisión de calderas; impuestos verdes; permisos ambientales vigentes y el Programa de Recuperación Ambiental y Social de la zona (PRAS).

Sostuvo que para la confección del inventario se utilizó la misma metodología implementada en el Plan de Huasco puesto que eran relativamente parecidos -en ambos casos existía una termoeléctrica de Gener y en uno había una fundición de hierro, en lugar de una fundición de cobre. Sin embargo el de Huasco, fue aprobado por la Contraloría, motivo por el cual, no existían indicios de que, en este caso, se iba a hacer objeción de la misma metodología que habían usado en una zona similar.

Sin embargo, afirmó que la elaboración del plan se hizo sobre la base de datos erróneos, por malos cálculos y cambios de unidades de medida al momento de fijar niveles de contaminación.

Manifestó que respecto a la modificación en la unidad utilizada para medir los gases contaminantes de las calderas, en particular el óxido de nitrógeno, se debió a que durante la elaboración del anteproyecto se propuso que el límite de emisión estuviera expresado en partes por millón, sin embargo, el límite máximo fue presentado en miligramos. Este cambio de unidad de medida bajo el objetivo de homologar las cifras para fijar los límites de contaminación, supuso multiplicar por dos los límites de las emisiones, lo que como resultado aumentó el límite de contaminación y que el plan de descontaminación finalmente no descontaminara. Agregó que del cambio de unidad “nadie se dio cuenta”.

Explicó que para disminuir la emisión de dióxido de azufre -otro de los gases contaminantes- se puso el foco en las calderas de las diversas plantas productivas y se alinearon con la normativa europea para esa tipología de fuente. Por lo tanto, se experimentó un aumento de 50 a 200 microgramos, en la categoría de mayores de 20 megavatios. Lo que dijo fue un error porque en el caso de la zona de Quintero. Puchuncaví, son muy pocas las fuentes que se encontraban en dicha categoría, representaban sólo el 0,8% de la emisión de dióxido de azufre, por lo que normarlas no significaba un impacto en el fenómeno de la contaminación.

Sostuvo que el inventario de emisiones plantea una forma de regulación que tiene que ver con el tonelaje anual emitido por una fuente, mientras que en paralelo, se presentan limitaciones en concentración. Indicó que dichas limitaciones en concentración, lo que hace es esencialmente evitar *peaks*, es decir, evitar que se supere cierto valor, en este caso, 50 microgramos en termoeléctricas ubicadas en cualquier zona.

Manifestó que si se observa la fuente real, se está cumpliendo con el estándar de 50 microgramos, no obstante, al modificarse a 30, todos esos peaks tienen que disminuir, es decir por efecto de cambiar de 50 a 30, se reduce la concentración, se tiene una disminución de emisiones.

Precisó que el planteamiento para la termoeléctrica, la reducción de emisiones no correspondía al tonelaje anual, sino que era dada por la disminución en las concentraciones.

Señaló que el tema de las calderas, constituye parte de la regulación, no obstante, advierte que si se observa el aporte de las calderas en el inventario de la zona, el SO2, es menor de 1%; en NOx es menor de 10% y en el caso del material particulado, bordea los 15%, por lo tanto, tanto las calderas como el grupo de fuente, no es particularmente significativo.

Explicó que los gases dentro del plan son precursores de material particulado, y que su participación es bastante menor en cuanto al material particulado total. En ese sentido, la modificación que se realizó tenía relación con dar coherencia y consistencia entre las normas internacionales y con el resto de los planes que se estaban presentando en otros lugares del país.

Expuso que la zona de la bahía de Quintero se encuentra en el borde entre la latencia y saturación, y que para salir de la saturación se debía bajar 0,3 microgramos y, tomar medidas en el plan nuevo de descontaminación concordantes con la realidad existente en dicho momento, la que corresponde a una saturación muy leve por sobre el límite.

Expresó que este tipo de instrumentos no evita los episodios de crisis, salvo que se incorporen medidas o desarrollen regulaciones para abordar episodios, o que se cuente con normas, con un desarrollo normativo que se haga cargo de los componentes causantes de la crisis, que hasta ahora no se ha podido esclarecer. Motivo por el cual, descartó que el plan constituya un instrumento preciso para evitar los episodios.

Puntualizó que la Contraloría objetó primero, que en el inventario se utilizó una metodología que hacía que las emisiones fueran más altas; segundo, las unidades en la regulación de calderas. Agregó que respecto de las unidades y los cambios de regulación de calderas ocurrieron entre el anteproyecto y el proyecto definitivo, y las razones son las que expuso. En el caso del inventario, señaló que llegaron al anteproyecto con un inventario y ese inventario no se modifica desde el anteproyecto hasta que la Contraloría representa.

Reiteró que la “modificación” o “adecuaciones” ocurrieron durante el proceso de recabar información técnica y científica para construir un anteproyecto, y ese proceso culminó con un inventario dentro del anteproyecto, inventario que se mantuvo, que no se modificó.

Estableció que esa construcción de inventario se hizo bajo la misma metodología que se había utilizado en Huasco, y ese fue aprobado por la Contraloría.

Indicó que no siente que está inhabilitado para trabajar en Enap, porque el Ministerio de Medio Ambiente no es el ente fiscalizador de las empresas, sino que más bien, es un regulador. Agregó que si se revisa el anteproyecto y el proyecto definitivo, se puede advertir que Enap era la empresa a la que se le hacían mayores exigencias.

42.- SEÑORA TANIA BERTOGLIO, EXSEREMI DEL MEDIO AMBIENTE REGIÓN DE VALPARAÍSO.

Manifestó que un plan de descontaminación tiene relación con llegar a los niveles normales de concentración de un componente específico que haya sido declarado saturado. Sin embargo no soluciona los problemas de contaminación en la zona, porque es un plan de descontaminación de un solo componente, que es material particulado y con ello no se soluciona la contaminación por hidrocarburos o por otros componentes, del suelo, y del agua.

Agregó que un plan de descontaminación nace como una propuesta de plan o una propuesta de anteproyecto que se difunde, pasa por un proceso de

participación, donde distintos actores, como la sociedad civil, organismos públicos, el mismo sector industrial, los mismos regulados y otros, participan entregando información y observaciones a este anteproyecto por lo tanto, después queda con las modificaciones.

Expresó que estuvieron durante los cuatro años en ese territorio, a través del Consejo de Recuperación Ambiental y Social, elaborando el Programa de Recuperación Ambiental y Social (PRAS), de Quintero-Puchuncaví, en que participaron todos los últimos jueves de cada mes y además iban en otras ocasiones, en sesiones extraordinarias, reuniendo información, implementando acciones en relación con lo que solicitaba la ciudadanía.

Indicó que por primera vez se levantó un diagnóstico participativo elaborado en conjunto con la ciudadanía, y uno de los temas allí señalados era la necesidad de un plan de descontaminación para calidad del aire, material particulado. Pero no solo eso, sino también el requerimiento de otras normas como la de dióxido de azufre horario, la de calidad del suelo para la bahía de Quintero. Por lo tanto, la calidad del aire es una de las tantas cosas que hay que solucionar. Sin embargo, hizo presente que la única forma de ver si está saturado o no un componente es teniendo normas y de ahí viene un plan de descontaminación o de prevención si está en latencia.

Aseveró que respecto del plan objetado por la Contraloría General de la República hicieron difusión cuando tuvieron el anteproyecto, una difusión anticipada en todos los territorios, y recogieron observaciones de la gente. Eso sí a nivel central se modificó sustancialmente el plan de descontaminación que terminó siendo rechazado, sin que acá se tuviera noticas de ello porque en algunos momentos la comunicación no fue tan fluida con el nivel central respecto de las modificaciones. Por ejemplo, sostuvo que, nunca se enteró de los datos que llegaron a última hora sobre calderas, porque revisando los antecedentes que en esa época difundieron en el territorio como Secretaría Regional Ministerial, eran los que realmente correspondían y después aparecieron otros, por razones que desconoce. Puntualizó que en las presentaciones que hicieron en el sector no tenían las cifras elevadas de las calderas. Estas eran bajas, incluso muy parecidas a las que hoy se ingresan en este nuevo plan.

Indicó que el anteproyecto y después el plan que fue rechazado no incorporaba la regulación de hidrocarburos volátiles, porque como no estaba normado y el tema ahí era material particulado, pero ahora lo están considerando por ser un precursor de material particulado. Agregó que para elaborar una norma de un componente tiene que haber un monitoreo con la misma metodología a lo menos tres años sobre cómo ese componente actúa en el medio ambiente. Explicó que una estación de GNL detectaba hidrocarburos, pero no había mediciones, entonces, no podían iniciar un proceso normativo de ese componente, sin embargo se hicieron la fiscalización de las empresas en cuanto a los hidrocarburos volátiles

Puntualizó que el año 2017 hubo en la bahía episodios de contaminación por hidrocarburos y encargaron un estudio que permitiera vislumbrar cuál era la fuente de contaminación. Añadió que durante varios meses en la zona estuvieron colocando estaciones de monitoreo y no solo de detección de estos hidrocarburos, sino que también una meteorológica para determinar entre la dirección del viento y las condiciones climáticas de dónde venía esa emisión. Se instalaron estaciones de monitorio en distintos sectores, tanto en Quintero como en Puchuncaví, incluso

pidiendo permiso a las empresas del sector y del parque industrial para instalar este instrumento, con la finalidad de determinar de dónde venía.

43.- SEÑOR PABLO BADENIER, EXMINISTRO DEL MEDIO AMBIENTE.

Manifestó que durante su gestión la Contraloría tomó razón de diez planes de descontaminación ambiental en el país. Sostuvo que ningún gobierno anterior, con los mismos datos de emisiones, había declarada saturada o latente la zona. La decisión se tomó con los monitoreos de los años 2012, 2013 y 2014 y se declaró el año 2015, con datos de monitoreo de hace tres años, porque hay que constatar la superación de normas de calidad que entran en estado de saturación o en estado de latencia.

Indicó que el decreto de saturación y latencia, de septiembre de 2015, declara que hay una zona saturada por material particulado fino, concentración anual, zona latente por material particulado fino, concentración de 24 horas, zona latente por material particulado grueso como concentración anual. Esa es la superación de normas de calidad que hoy tienen Concón, Quintero y Puchuncaví. La zona saturada es de 20,3, siendo la norma de 20 microgramos por metro cúbico normal de aire.

Manifestó no estar de acuerdo con la representación del Contralor dado que a su juicio este plan sí descontamina, asegurando que las observaciones eran subsanables.

Señalo que el inventario de emisiones de 3 de mayo de 2016, fue parte del anteproyecto que se sometió a consulta pública y presentado al Consejo de Ministros para sustentabilidad y es el mismo al que se llegó a diciembre de 2016. Recalcó este punto para que se comprenda el alcance del dictamen que representa el plan por el Contralor General de la República. Añadió que el documento dice que los niveles de emisión consignados en el inventario de emisiones establecido en el artículo 2, de la tabla 2, en lo que se refiere a fuentes puntuales, AES, ENAP, Codelco y otras puntuales (DS 138) como el grupo de calderas, son superiores a las que constan en el informe técnico contenido en el respectivo expediente electrónico, habiendo sido modificado mediante una estimación efectuada por la Secretaría de Estado.

Aseveró que en ninguna parte dice que se cambiaron los inventarios. Lo que dice es que en un informe técnico, el AGIES, Análisis General de Impacto Económico y Social, utilizó otros datos para estimar los costos y beneficios del plan, pero el inventario que se sometió a consulta pública fue el mismo que llegó en el plan aprobado por el Consejo de Ministros. Explicó que el AGIES se construyó con emisiones reales de 2013 lo que habría que preguntarse es si fue un año representativo desde el punto de vista de la operación, de las emisiones que hubo en ese año en particular.

Entonces, desde el punto de vista metodológico legítimamente existen distintas metodologías para construir un inventario de emisiones y sobre él ir generando reducciones porcentuales. Lo que se hizo en el inventario de emisiones del plan que fue representado por la Contraloría General de la República efectivamente fue un límite superior potencial de emisiones autorizadas, sea por los decretos 13 o el 28, o por una Resolución de Calificación Ambiental, y sobre ese límite se generan reducciones porcentuales.

Reiteró que el anteproyecto y el plan tienen el mismo inventario de emisiones, y las emisiones que son distintas son las emisiones del AGIES, no de los inventarios.

En cuanto a las calderas puntualizó qué hoy no están normadas y que de manera particular, se ha normado en función de un plan de descontaminación, pero no hay una norma nacional de calderas que emiten más o menos lo que estiman.

Los límites máximos de emisión para calderas son superiores a los previstos en el anteproyecto, en particular en lo que atañe a óxidos de azufre y a óxidos de nitrógeno, no existiendo antecedentes fundantes para que sobre la base de un mismo inventario de emisiones se modifiquen las medidas posteriormente aprobadas en el plan.

Primero, declaró, que es razonable, incluso, hasta esperable, que existan modificaciones entre el anteproyecto y el proyecto que se somete al Consejo de Ministros para la Sustentabilidad, porque el anteproyecto es el que se somete a consulta pública, el que recibe observaciones de los regulados, de la ciudadanía, de los alcaldes. Por lo tanto, es razonable esperar que haya cambios.

El anteproyecto que se somete a consulta pública en el marco de emisiones de calderas, son del orden del 8 por ciento de las emisiones de este plan de descontaminación. Probablemente las emisiones de SOx y NOx se controlan, porque son precursores de material particulado; no es porque se está superando normas ni de NOx ni de SOx. Hay estimaciones académicas que del orden de un 25 por ciento de esas emisiones son precursores efectivos de material particulado grueso o fino, dependiendo de las características de la atmósfera en ese momento. Esto lo mencionó porque en las normas de emisión de calderas hay límites máximos para material particulado; límite máximo para óxidos de azufre; límite máximo para NOx. Y efectivamente hay cambios que no son menores, haciendo la salvedad de lo que representan porcentualmente del inventario y las emisiones de NOx y SOx que tienen que ver con controlar un precursor de material particulado. Ese es el objetivo de controlar NOx,

Indicó que acá se produce el primer cambio: hay una norma más exigente de material particulado en el proyecto final; es más exigente que la norma que se sometió a consulta pública, que es material particulado, contaminante por el cual hay un nivel de saturado latente. No obstante, al parecer, hay unos cambios, por los dichos del Contralor, no del todo justificados, en emisiones de SOx para calderas existentes y límites máximos de NOx para calderas existentes.

Expresó que el anteproyecto que reingresó a la Contraloría el 13 de diciembre de 2016, sí tiene un cambio de unidad -esto es partículas por millón en volumen, desde microgramos por metro cúbico normal y que tiene un factor de conversión. Por lo tanto, efectivamente hay varios cambios en la tabla que regula los límites máximos de emisiones de calderas nuevas y existentes.

Los cambios son la disminución del límite máximo para la emisión de material particulado para calderas nuevas; aumenta el límite máximo de SOx para calderas existentes; aumentan los límites máximos de NOx para calderas nuevas y existentes -en todos sus tamaños-, y, finalmente, se detecta y corrige, en el trámite de toma de razón de la Contraloría, la unidad de medición de mg/m3 a partículas por millón en volumen.

Chile no tiene normas de emisión para calderas. Por lo tanto, lo que se hace en esta zona es ir regulando las calderas de Concón, Quintero y Puchuncaví; las calderas de Valdivia, las calderas de Curicó. Agregó que en el anteproyecto de normas de emisión para calderas se observa un grado más de sofisticación -por decirlo de alguna manera- donde, además del tamaño de la caldera, se norman las emisiones y si los combustibles son gaseosos, líquidos o sólidos.

Por lo tanto, esta norma viene a corregir las particularidades de normar calderas por intermedio de un plan de prevención y descontaminación atmosférico. Si se tiene un PPDA y se tienen calderas en la zona declarada saturada latente obviamente el PPDA es un instrumento para regular esas emisiones ante la ausencia de una norma nacional de emisión de calderas.

Por consiguiente, de buena fe creé que ahí está el origen, y no es un número mágico e indicó que bastaba con revisar los planes aprobados por la Contraloría solo dos o tres meses antes, para verificar que son los mismos valores de las calderas en años anteriores.

Por último, llamó a tipificar el delito penal ambiental, en razón de lo sucedido de con la contaminación en la bahía de Quintero

44- SEÑOR BORIS CHAMORRO REBOLLEDO, ALCALDE DE CORONEL.

Se refirió a que cada localidad de estas mal llamadas zonas de sacrificio tiene una característica o una particularidad, por ejemplo en la ciudad de Coronel se ha detectado –no solo en estudios realizados por el municipio, sino por el Instituto de Salud Pública (ISP)-, en el organismo de los niños y las niñas de establecimientos educacionales, la presencia de metales pesados. Específicamente, en aquellos que están más cerca de las unidades generadoras de energía o termoeléctricas. De ahí que Por eso el proceso de industrialización descarnado de la ciudad de Coronel no tiene nada que envidiar a lo que ocurre en Quintero o Puchuncaví.

La industria de generación energética ha aumentado 9,7 veces el consumo y combustión de carbón, en Coronel existen 4 plantas termoeléctricas y la termoeléctrica más antigua de Chile y el mundo que cumplió su vida útil, operan 6 terminales portuarios que movilizan 8 millones de toneladas, duplicando lo que se transfería en el 2006, La industria manufacturera pesada ha crecido en 114% en 10 años con 300 empresas (cementeras, astilladoras, forestales, 3 parques industriales, etc.). La industria pesquera ha crecido 45% en los mismos 10 años, con 8 pesqueras, que provocan contaminación ambiental por olores.

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Expresó que el 16 por ciento de la producción nacional de energía a carbón se concentra en la ciudad de Coronel en un radio de 3 kilómetros a la redonda. Es decir, 16% de la energía que consumen los chilenos se desarrolla y se genera en la ciudad de Coronel, en un radio de 3 kilómetros, en pleno casco urbano de la ciudad y alrededor de 3 kilómetros de 10 establecimientos educacionales que albergan a más de 3.000 estudiantes, aproximadamente.

Señaló que en el casco histórico de la ciudad de Coronel hay 27 calderas que generan 8.800 toneladas de dióxido de nitrógeno anuales y 8.700 toneladas de dióxido de azufre en un radio de 3 kilómetros, estos según un informe del Ministerio de Salud del año 2016; es decir, 1.406 toneladas de MP 2,5, según la fuente del Ministerio de Medio Ambiente, en febrero de 2018.

A todo esto se le suma el único vertedero de cenizas en el mundo emplazado en el casco urbano de una ciudad, como es en Coronel y que pertenece a la central termoeléctrica Bocamina. Afirmó que en este mismo lugar se ubica

Agregó que en el año 2010 por la aprobación de la Resolución de Calificación Ambiental (RCA) se autorizó la ampliación del vertedero de cenizas y que más encima entre 2010 y 2018 ha aumentado en 51 veces su tamaño, con un consumo y combustión de carbón de 2 millones ton/año, con 190 mil ton/año ceniza y un tráfico diario de 1760 ton/diaria de cenizas.

En la misma línea, sostuvo que según datos del departamento de educación municipal entre los años 2012 y 2017 se observa un crecimiento exponencial en niños con espectro autista, con una curva ascendente hasta 2017. Agregó que la exposición a agentes contaminantes por la población no son ha provocado el aumento de niños con necesidades educativas especiales, sino que también el incrementó de enfermedades.

En el año 2013 la Policía de Investigaciones hizo un informe pericial que detectó en la bahía de Coronal metales pesados, como arsénico, cadmio, mercurio, cromo, plomo, zinc y cobre. Esto se repite en 2016, donde la Seremi de Salud, a través del ISP, detecta la presencia de metales pesados en 18 niños, lo que provino de una muestra de 285 escolares de 15 establecimientos educacionales de la ciudad, principalmente arsénico, cadmio, mercurio y níquel.

Así los habitantes de la comuna de Coronel quienes a través del actuar de Endesa se ven expuestos a convivir en .la .comuna que habitan con altas concentraciones de arsénico, cromo, cinc, mercurio, plomo y vanadio, metales que individualmente considerados son nocivos para la salud de las personas y por consiguiente lo son aún más, en su conjunto, con efectos progresivos en el tiempo.

Respecto de tales sustancias, mencionó que sus efectos en la salud de las personas de acuerdo a la Organización Mundial de la Salud (OMS) pueden ocasionar los siguientes efectos:

a) Mercurio: constituye uno de los diez grupos de productos químicos con mayores repercusiones en la salud pública de acuerdo a la OMS, siendo una sustancia tóxica con efectos nocivos para el ser humano y en especial para .las embarazadas, lactantes y los niños, generando alteración en el sistema neurológico.

b) Plomo Entre los principales efectos tóxicos que produce en las personas figuran la anemia, trastornos neurológicos e insuficiencia renal.

c) Vanadio: Esta sustancia en forma de polvo o humo, como acontece en la especie, penetra con facilidad en el organismo a través del tejido pulmonar.

d) Arsénico: La exposición prolongada al arsénico a través del consumo de agua y alimentos contaminados puede causar cáncer y lesiones cutáneas. También asociado a desarrollo de enfermedades cardiovasculares, neurotoxicidad y diabetes.

Sostuvo que el medio ambiente está siendo afectado en toda su extensión a través del depósito en el suelo de Coronel de grandes cantidades de carbón (materia prima de la central termoeléctrica Bocamina para generación de energía) cuyos componentes tóxicos a través de un proceso de han trascendido y contaminado las aguas subterráneas y a través de este mismo proceso otra cantidad de sustancias han ido a desembocar en el mar causando la contaminación de algas cuya

consecuencia directa es que a. su vez afecten toda la cadena trófica marina además de causar graves impactos a la salud de las personas con su consumo. Sostuvo que hay personas que viven en una zona aledaña a Bocamina, que no cuentan con alcantarillado, lo cual les genera una sobre exposición a los contaminantes indicados, toda vez que consumen aguas de pozos que se encuentran contaminadas y cuyo hervor no elimina las sustancias tóxicas, además de tener que convivir con una atmósfera contaminada respirando y absorbiendo por vía cutánea .la toxicidad del mercurio, arsénico, plomo, cadmio, vanadio, etc.,

Indicó que Quintero y Puchuncaví es noticia nacional, producto de que se detecta alerta amarilla por emergencia ambiental, con 133 afectados. Pues bien, Coronel también es noticia nacional en virtud de que se encuentra, después de cinco años de estudios de suelo, aire y mar, que la mayor concentración de metales pesados está en el vertedero de cenizas.

Sostuvo que Coronel también es parte de una red de municipios mal catalogados como zonas de sacrificio. Agregó que es una opción agruparse de manera colectiva, con Til-Til, Quintero, Puchuncaví y Huasco, para hacer entender al Estado que debe tomar conciencia y que estas industrias, nocivas para el medioambiente y la salud, han provocado múltiples enfermedades a los habitantes de estas comunas.

45.- SEÑOR CRISTIAN RUIZ, MIEMBRO DE LA COORDINADORA SOCIOAMBIENTAL CORONEL DESPIERTA.

Indicó que Coronel participa y produce 16 por ciento de la matriz energética del país pero hay que tomar en cuenta el costo que ello significa.

Manifestó que el Estado -y los gobiernos de turno-no garantiza a los habitantes de esta comuna el derecho a la vida, a la salud, a vivir en un lugar libre de contaminación y la igualdad ante la ley, privilegiando el desarrollo económico por sobre la vida de la población. En efecto, afirmó que el Estado y sus autoridades políticas tanto al Poder Ejecutivo como Legislativo, han actuado de forma negligente originando con ello las llamadas zonas de sacrificio.

Expresó que la Superintendencia de Medio Ambiente ha actuado con un traje a la medida para estas empresas, creando una normativa laxa que permite vulnerar los derechos fundamentales, y permiten tener emisiones contaminantes, que en el caso de Coronel superan el 400 por ciento de lo permitido por la norma de la Organización Mundial de la Salud. Indicó que presentaron dos denuncias ante la Superintendencia de Medio Ambiente, una por la violación de la norma de emisión de las termoeléctricas, y la otra por elusión de la RCA, por el tendido eléctrico de Transelec que puso en servicio la subestación Lagunillas, que alimenta el sistema interconectado de Bocamina I, termoeléctrica que ya tiene 48 años de funcionamiento. Al respecto indicó que ninguna autoridad ha sido capaz de poner fin a la contaminación que provoca esta central antigua y obsoleta, como otras tantas que se ubican en Huasco, Mejillones, es decir el modelo económico permisivo se replica en todo Chile.

Sostuvo que en Coronel existen muchas otras industrias, como la pesquera, la química, forestal o cementera, que podrían asociarse a la contaminación ambiental, del suelo, del mar, del agua dulce y de los espejos de agua de los que se abastece la comuna.

Agregó que, la combustión del carbón en el proceso de generación eléctrica produce como desecho grandes volúmenes de cenizas, las que contiene químicos como oxido de sílice, aluminio, hierro, calcio y metales pesados. Sin embargo, en Chile y como es de esperar, con el traje a la medida que supone la normativa medioambiental para este tipo de empresas, estas cenizas no son consideradas residuos peligrosos en el marco del decreto supremo N° 148, de 2003, del Ministerio de Salud, no obstante esto es evidente que los metales pesados sí constituyen riesgo y daño para la salud de las personas en altas concentraciones.

Sobre el vertedero de cenizas, precisó que se encuentra a rajo abierto, por lo que hay una polución generalizada, con lo que la contaminación se desparrama y difumina a 30 kilómetros a la redonda al menos. El informe de la BIDEMA, luego de una investigación que duró 4 años, determinó la presencia de metales pesados en 21 personas de la comunidad estudiantil de la Escuela Rosa Medel de Coronel y concluyó un nexo causal, entre metales pesados, que son el mercurio, el plomo, el arsénico, el cadmio y la termoeléctrica a carbón Bocamina 1y también la permeabilidad de los metales pesados a las napas subterráneas, y al mar inclusive.

Agregó que desde mediados de los años 80´s que se vienen realizando estudios que muestran graves impactos en la salud de los niños, sin que se tomen las medidas de seguimiento y de prevención necesarias. Incluso en un caso, que mostraba graves mutaciones genéticas precursoras del cáncer en la población de Puchuncaví, sencillamente no se pagó ni recepcionó el estudio. Indicó que es claro que en Chile existe una cantidad suficiente y significativa de estudios “científicos” concluyentes -y una importante cantidad de estudios exploratorios y/o preliminares – que demuestran los graves impactos, efectivos y potenciales, que desde hace décadas han tenido las termoeléctricas a carbón en la salud de los niños de las comunidades circundantes

Advirtió la necesidad del congelamiento del parque industrial en Coronel, ya que esta es una zona saturada, desde la puesta en marcha, el año 2012, de las dos nuevas centrales termoeléctricas, que es Bocamina 2 y Colbún Santa María.

También exigió el rechazo a la explotación del mar con la industria salmonera, porque sus operaciones la hacen a costa de la contaminación sistemática del fondo marino con antibióticos, la desaparición de la fauna endémica producto del escape de salmones y el deterioro de la pesca artesanal en el territorio.

La comuna de Coronel casi desde sus inicios, está asociada a la actividad industrial. De hecho, ya lleva más de 150 años con esa actividad, sin embargo no siempre fue una zona de sacrificio. En efecto en la última década del siglo XX, a principios de los 90, ante las consecuencias sociales y económicas que produciría el inminente cierre de las minas del carbón, los yacimientos de Schwager y de Lota, se incentivó la creación de los parques industriales y llegaron diversas industrias a asentarse en el territorio: pesqueras, fábricas de harina de pescado, aserraderos, empresas químicas, la instalación del Puerto de Coronel, centrales termoeléctricas, una cementera escasos metros de establecimientos educacionales, y otras actividades productivas diversas, y con ellos la contaminación. Todas estas instalaciones han impactado de diferente forma el medio ambiente de la comuna, producto del aumento de emisiones de gases contaminantes a la atmósfera (fundamentalmente material particulado y dióxido de azufre), generación de ruidos molestos, explotación intensiva de recursos pesqueros y acuícolas, vertido directo de

residuos líquidos y sólidos y efluentes industriales al mar, succión de agua marina y emisión de riles, y emisión de residuos de terminales y puertos pesqueros.

En la década siguiente se anunciaría la construcción de dos nuevas centrales termoeléctricas: Colbún Santa María y Bocamina 2, que terminarían de consagrar a Coronel como una ciudad saturada de contaminación y como zona de sacrificio.

Indicó que en la zona hay 4 termoeléctricas, 27 calderas, al menos 9 pesqueras que han crecido en torno al 46 por ciento, gracias a la ley de Pesca, 6 terminales portuarios, carbonero, graneles, contenedores, forestales y, entre ellos, un puerto químico de propiedad de Oxiquim, misma empresa que también se encuentra emplazada en Quintero. Hay 300 empresas en tres etapas de parques industriales, 70 por ciento del suelo ocupado por plantaciones de forestales de monocultivo, un crecimiento del 40 por ciento del suelo y con fines habitacionales desde 2010, con la coyuntura del terremoto, construyendo las inmobiliarias sobre humedales inclusive. Aseguró que este aumento del mercado inmobiliario en una zona saturada por la contaminación es absurdo, o sea, está llegando más gente a morir a Coronel por la silenciosa acumulación de metales pesados en los pulmones.

Se producen 2 millones de toneladas de carbón al año y son quemada y enviadas sus cenizas a la atmósferas, 1.406 toneladas de material particulado 2,5, según el Ministerio de Medio Ambiente en febrero de 2008. Producto de todo ello hay más de 60 casos de niños con espectro autista, asperger, en la educación municipal solamente, esto se asocia a la exposición prenatal a metales pesados, según un estudio realizado en Vancouver, Canadá, y según lo sostenido por el propio municipio y su departamento educacional. Según estudios del departamento de Salud de Coronel, aumentó la incidencia en 32% de enfermedades renales crónicas, de enfermedad pulmonar obstructiva crónica en un 15% cáncer de pulmón, 50 %; cáncer de piel, 58 %; abortos espontáneos y el aumento en el 26 % de las consultas por salud mental. Aseguró que la comuna tiene 9% de cesantía, según el informe del INE, no obstante que el 16% de producción energética de Chile se produce en Coronel.

Indicó que el Gran Concepción es zona latente de contaminación y el 75 % de la contaminación del Gran Concepción es producido en Coronel,

Este vertedero de cenizas a rajo abierto tiene la concentración más grande de arsénico, cadmio, níquel, plomo, cromo, que, alcanzando parámetros elevados como nunca antes. Esto se logró medir con instrumentos especializados y de precisión como microscopios de última tecnología para determinar qué tan cierta era la contaminación.

Señaló que las termoeléctricas a carbón en Chile constituyen el principal agente de contaminación atmosférica local y la mayor fuente de contaminación global. Estos son datos de la Organización Mundial de la Salud por la combustión de carbón, problema que es urgente resolver con la mayor celeridad para proteger la salud de la población, los ecosistemas y las economías locales, así como también cumplir los compromisos asumidos por Chile para enfrentar el cambio climático global en el marco del Acuerdo de París. A este impacto sobre los ecosistemas costeros se suma la descarga al mar de aguas calientes y con químicos antialgas, luego del uso para enfriar las turbinas. Ello, obviamente, altera de manera radical las comunidades de flora y fauna de los ecosistemas marinos en las áreas de descarga generando graves

consecuencias para las economías locales de pescadores artesanales y de mariscadores, entre otros.

En definitiva señaló que como organización exigen: (i) la suscripción a la brevedad del Acuerdo de Escazú, que asegura participación democrática en la toma de decisiones para la instalación de proyectos industriales en cada zona; (ii) la inmediata homologación normativa con los estándares internacionales establecidos por la Organización Mundial de la Salud y europeos; (iii) el compromiso transversal de todos los responsables en la toma de decisiones, para que las empresas que no cumplan los estándares se cierren a la brevedad; (iv) detener el crecimiento del parque industrial de Coronel; (v) restablecer a la brevedad la norma para arsénico y todas las normas necesarias para la calidad del aire; (vi) implementar tecnología de punta en todas y cada una de las plantas que operan en el parque industrial de Coronel; (vii) cierre inmediato de las termoeléctricas a carbón; (viii) que la medición de las emisiones de las empresas deje de ser bajo el estándar individual y se establezca una norma de medición que considere la sumatoria de las emisiones de todas las empresas del parque industrial, reconociendo que la mezcla de los gases emanados y de las emisiones contaminantes provoca una reacción química altamente peligrosa para la salud de las personas y para la biósfera; (ix) que el sistema de monitoreo de calidad del aire sea vigilado por la sociedad civil y no por las propias empresas que producen las emisiones, a través de un consejo de vigilancia de la calidad del aire para alertas tempranas; (x) que todos y cada uno de los habitantes afectados con la nube tóxica, en el caso de Quintero, sean cubiertos en todos sus requerimientos para reintegrarse a su vida cotidiana; y (xi) que se haga un seguimiento para pesquisar los efectos a largo plazo sobre las funciones hematológica y hepática derivados de la presencia de metales pesados.

Además de esto se requiere a la brevedad médicos especialistas, pediatras, oncólogos, broncopulmonares, geriatras, médicos internistas, médicos salubristas y ginecólogos y la inmediata capacitación del equipo médico del hospital de Coronel y de los consultorios de la comuna en conocimientos técnicos y médicos para atender emergencias toxicológicas masivas, contando con los insumos y equipos tecnológicos adecuados para atender con rapidez y precisión.

Solicitó que se cumpla el compromiso final de la realización de exámenes y tratamientos de por vida a todos los afectados por la contaminación en Coronel por el Estado, de modo que deje de ser cómplice y se transforme en protagonista de la recuperación de la salud.

Concluyó exigiendo el cierre definitivo de Bocamina I, que ya lleva 48 años en operaciones, y del vertedero de cenizas propiedad de la empresa Enel que contamina el aire que respiramos y que es el único que está emplazado en el casco urbano de una comuna a nivel mundial.

46.- SEÑORA DORIS ZAMORANO DEL CONSEJO PARA LA RECUPERACIÓN SOCIAL Y AMBIENTAL DE HUASCO.

Señaló que la comuna de Huasco se localiza en el sector costero de la Región de Atacama con una población de 10.595 habitantes. El valle del Huasco está unido por la cuenca del río Huasco conformada por las comunas de Huasco, Freirina, Vallenar y Alto del Carmen, en la parte alta, con una población total de 77.737 habitantes. Sus actividades productivas dominantes han sido la pesca en la parte costera y luego la agricultura.

Destacó que esta agricultura es de nicho y tiene características únicas. Tiene un clima muy similar al del Mediterráneo con los mejores cielos del hemisferio sur; su flora y su fauna es conocida más que nada por el Desierto Florido. El suelo, el aire, el agua y la dulzura de sus frutos le dan un toque a la parte agrícola.

Explicó que el 0,4 por ciento de la superficie del territorio de la Región de Atacama es agrícola. Por lo tanto, un porcentaje de 99,6 por ciento puede destinarse para la Minería o para cualquier otra actividad, y a raíz de esto, la mayoría de los problemas que tienen Huasco se deben a la alta contaminación por la presencia de industrias que se abocan a contaminar y usar ese 0,4 por ciento como el Complejo Termoeléctrico Guacolda –con cuatro unidades a carbón en funcionamiento y otra pronta a inaugurarse - y la planta de pellets de hierro de la Compañía Minera del Pacífico.

Señaló que los tipos de contaminantes que existen son material particulado sedimentable con fierro, que afecta al sector agrícola; material particulado respirable, MP10-MP 2,5 y gases quimiotóxicos como SO2, NOX, CO2, entre otros.

Agregó que en la Bahía de Chapaco existen relaves que van al mar, residuos industriales que afectan al sector pesquero artesanal; también existe contaminación acústica, porque el tren pasa casi por todo el valle.

Consideró que, a raíz de la contaminación existe no sólo un deterioro global de la calidad de vida de los habitantes de la región, sino que también afectado a la salud de las personas, dañado la agricultura y pesca en la zona de Huasco, y producido zonas de sacrificio.

Recalcó que se ha producido una progresiva muerte de las economías locales como la pesca y la agrícola, que son fuentes laborales tradicionales que se desarrollaban mucho antes de que llegaran las empresas y que se han ido apagando hasta llegar a la cesantía por disminución de producción. Como consecuencia de esto muchos dueños de terrenos agrícolas han tenido que vender para que se construyan parcelas de agrado, porque han bajado tanto sus recursos económicos que no les alcanza para pagar a los trabajadores. Indicó que las características agrícolas de la zona de Freirina permitían que se desarrollaren actividades económicas como la producción de aceites y aceitunas con denominación de origen.

Sostuvo que al igual que las otras zonas de sacrificio, Huasco es una comunidad pequeña, pobre y con escasa capacidad de reacción ante un séquito de técnicos y de personas que tienen la habilidad de dar vuelta la imagen de una empresa, dando a entender que todo se hará en beneficio de los habitantes, pero en el fondo trae más pobreza.

Agregó que estas empresas se ubican en la costa hay muelles de embarque y, en el caso de Huasco, hay desalinizadoras, están cerca de centros energéticos, líneas férreas y conectividad, porque una débil legislación ambiental permite a las empresas decidir dónde instalarse, qué combustible usar y cuánto contaminar.

Señaló que la Planta de Pellets de CMP y la Termoeléctrica Guacolda son las principales fuentes emisoras de material particulado respirable MP10 y esta contaminación provocó que en mayo de 2012 la comuna fuera declarada como zona

latente por material particulado respirable en 2011 por el Ministerio del Medio Ambiente, considerando que las concentraciones de material particulado grueso (MP10) se encuentran entre un 80% y un 100% del valor de la norma de calidad primaria anual.

Destacó que el valle se encuentra ocupado por industrias intensivamente desde hace más de 30 años, siendo uno de los hitos industriales más importantes, la construcción de la planta de pellets de hierro de la Compañía Minera del Pacífico en 1978 – es decir lleva cuarenta años vertiendo relaves al mar- y a partir de los años noventa, se intensificó la puesta en marcha de centrales termoeléctricas y mineras.

Si bien ninguna de esas plantas sobrepasa los niveles de dióxido de azufre (SO2), la sumatoria de ellas señala que diariamente, en cambio, se emiten 118,2 toneladas de CO2, que corresponden 10,2 a la CMP y 108 a Guacolda. En síntesis sostuvo que el Valle del Huasco en la actualidad se encuentra comprometido desde sus montañas hasta su desembocadura, donde importantes proyectos de inversión han explotado con intensidad el agua del río Huasco, perjudicando a los habitantes de la zona.

Hizo presente que la planta peletizadora de hierro produce contaminación a la atmósfera y a los suelos con material particulado y gases quimiotóxicos, además de realizar evacuaciones al mar en ensenada "Chapaco" de residuos industriales, lo que ha significado un grave daño al ecosistema marino. Cuenta con dos chimeneas, una con filtro y otra, que hasta la fecha, transcurrido cuarenta años, sigue sin filtro. Tiene canchas de acopio de material sin domo, a pesar de los vientos característicos del valle. Donde está la empresa el viento toma lo que arroja la chimenea y lo lleva directamente hacia el pueblo, a la comuna de Huasco.

Por otra parte, Guacolda opera desde 1994. También aporta MP10, MP 2,5, SO2, NOX y otros metales que no se miden, lo que también ha llevado a la saturación y a la latencia, y en noviembre de 2017 aumentó su capacidad en 24 megawatts.

Mencionó que con el reconocimiento transversal del Presidente Piñera en su primer mandato, y de la Presidenta Bachelet, en su segundo mandato, en Chile existen zonas devastadas ambientalmente por la concentración de proyectos mineros y energéticos, altamente contaminantes. Agregó que el Ministerio de Medio Ambiente inició el Programa de Recuperación Ambiental y Social. (PRAS) en localidades de Chile identificadas por el propio gobierno como zonas de sacrificios, estas son: Tocopilla y Mejillones en la Región de Antofagasta, Huasco en la Región de Atacama, la Bahía de Quintero-Puchuncaví en la Región de Valparaíso y Coronel en la Región de Biobío.

Comentó que en la comuna de Huasco se da inicio a este proceso el año 2014 y su objetivo es recuperar ambientalmente el territorio y mejorar la calidad de vida de los habitantes. Se convoca para participar en la elaboración del Programa a un “Consejo para Recuperación Ambiental”, formado por 14 integrantes de la sociedad civil, de la empresa CMP, de la termoeléctrica Guacolda, y autoridades del gobierno local, provincial y regional.

Las principales demandas de la sociedad civil realizadas en las mesas de trabajo durante la ejecución del PRAS y durante este año son:

1) Que los valores máximos de contaminantes normados se ajusten a las referencias de la OMS.

2) Que las estaciones de monitoreo estatal para la calidad del aire sean discretas, continúas, con certificación EPA, que se realice análisis periódicos para determinar la presencia de metales pesados en el material particulado respirable y sedimentable, que se incorpore el monitoreo de hidrocarburos aromáticos policíclicos y que la información obtenida en las estaciones de monitoreo entregue datos de calidad del aire en tiempo real, para optimizar la toma de decisiones y entregar información precisa a la comunidad.

3) Que se fiscalicen las empresas no sujetas a Resolución de Calificación Ambiental.

4) Que en la normativa de planes de prevención y descontaminación se utilice línea base real; que las emisiones de proyectos en operación y aprobados sin operar no compensen emisiones entre empresas y que se establezcan sanciones en caso de no cumplir con las medidas propuestas para descontaminar.

5) Que el PRAS se haga cargo de evaluar el comportamiento y formación de compuestos sinérgicos, por el que actualmente nadie responde.

6) Que se considere en la modelación del aire, la formación de elementos secundarios como nitratos y sulfatos, precursores de lluvia acida y de otros compuestos que se forman en los territorios donde se concentran proyectos diversos.

7) Que en materia de salud se aplique la norma del plomo, vigente desde el año 2001, que estipula realizar examen en sangre a niños menores de 2 años y ratificar el Convenio de Minamata para reducir el impacto por contaminación de mercurio; intensificar y expandir el monitoreo de la carga corporal de mujeres y fuentes alimenticias y realizar estudios financiados por el Estado.

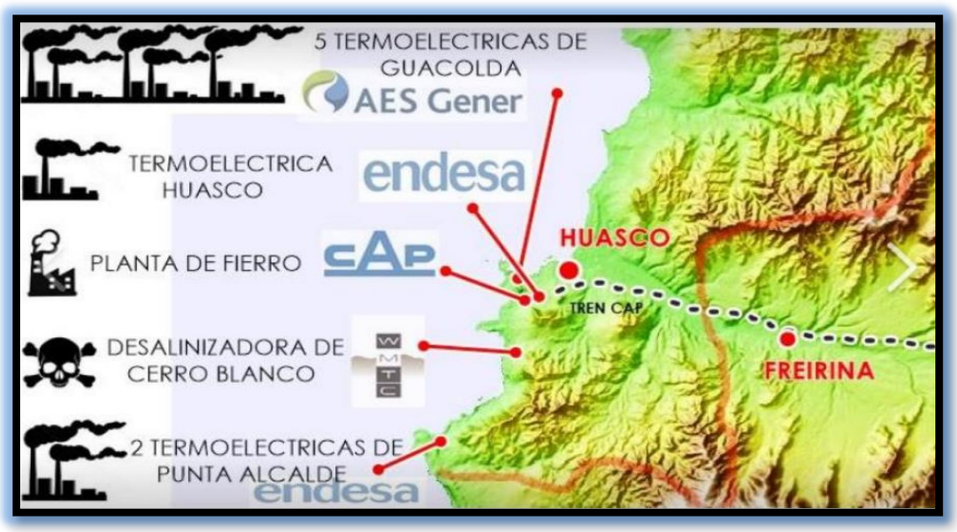
8) Contar con una Defensoría Ambiental Ciudadana de cargo del Estado, fomentar espacios de participación ciudadana que sea vinculante y resolutiva, para aportar en el mejoramiento de la calidad de vida en los territorios.

9) Que se incluyan políticas públicas para el cierre de termoeléctricas para descarbonizar las zonas de sacrificio y el resto del país.

47.- SEÑORA SOLEDAD FUENTEALBA, INTEGRANTE DE LA AGRUPACIÓN BRIGADA SOS DE HUASCO.

Respecto de los proyectos que existen para la comuna, indicó que hay 5 termoeléctricas de la empresa Guacolda-Aesgener; una planta peletizadora de fierro de la Empresa CAP; una desalinizadora de Cerro Blanco que está aprobado, pero sin funcionar y cuyas minas estarán instaladas en la comuna de Freirina, y dos termoeléctricas en Punta Alcalde de Endesa, proyecto que también está aprobado y sin funcionar, pero con RCA vigente.

Mencionó que, además, hay 3 puertos marítimos: Las Losas, que es de CAP y de Agrosuper; Guacolda I, que es de la empresa CAP y Guacolda II, que es de Guacolda-Aesgener.



Sostuvo que el año 2018 se aprobó una megaplanta desalinizadora de Aesgener, pero no para uso de sus termoeléctricas, porque ya son once las desaladoras, sino que para venta a terceros; o sea, cambió su giro de energía a agua con una simple declaración de impacto ambiental y no con un Estudio de Impacto Ambiental.

Indicó que los habitantes de esa zona están en riesgo de contraer cáncer en cualquier momento ya que existen pruebas suficientes para determinar que la exposición a la contaminación del aire causa cáncer de pulmón. El material particulado (MP), que es un componente importante de contaminación del aire exterior, es también clasificado como carcinógeno para los humanos.

Informó que la mortalidad por enfermedades cardiovasculares en la comuna de Huasco entre los años 2002 y 2013 fue la más alta de la Región de Atacama; la mortalidad por cáncer a los órganos respiratorios entre el año 2002 y el 2013 duplicó su porcentaje a nivel regional; la mortalidad por cáncer a las vías urinarias triplica su aumento en comparación con la región y se asocia a lo que determinan las estadísticas que declara la Organización Mundial de la Salud. Agregó que en el año 2015 el Ministerio de Salud realizó un estudio de evaluación de exposición a metales pesados en población infantil entre 5 años y 14 años. La evidencia preliminar es que hay niños con elevados niveles de arsénico y níquel.

Comentó que el año 2017 se realizó una evaluación del polvo negro en la comuna, y una de las conclusiones fue que la superación de valores guía para evaluación de medios ambientales (EMEG) para infantes y niños son superiores en cadmio, cromo, cobre, manganeso y vanadio. Además, se concluyó que el material particulado fino llega hasta el interior del valle. Otro estudio determinó que existe un patrón consistente con niveles más altos de exposición a níquel en niños de las escuelas en las ciudades que tienen una planta de energía alimentada por *petcoke*.

Manifestó que un estudio realizado en el año 2016 sobre mortalidad y morbilidad en las zonas con población expuesta a la quema carbón entre las que se incluyó a Huasco, concluyó que la mortalidad general más elevada es específicamente por enfermedades cardiovasculares y por cáncer, y que la mayor

cantidad de hospitalizaciones es por enfermedades cardiovasculares, cáncer y enfermedades respiratorias.

Afirmó que son dos las empresas responsables de producir el 99 por ciento del material particulado en Huasco la Planta de Pellets de Fierro de CMP, que solo a partir de 2010 comenzó a ser fiscalizada sobre el cumplimiento de la Resolución Ambiental, y las cinco plantas termoeléctricas de AES Gener la primera de las cuales comenzó a operar en 1995 y la última el 2010 cuya ampliación se realizó el año pasado.

Indicó que la contaminación superó los niveles de emisión permitidos en la normativa vigente y Huasco estuvo en situación de saturación, pese a lo cual nunca fue declarada zona saturada. Desde 2006 el nivel de emisiones ha disminuido, pero manteniéndose en situación de latencia, pues jamás se ha producido una baja significativa y constante en las emisiones porque los niveles de emisión suben y bajan. A raíz de ello fue declarada zona latente por material particulado respirable MP10 en 2012, pese a lo cual recién en 2014 se inició el proceso para aplicar el plan de latencia para lo cual se contrató una consultora, DICTUC (*Dirección de Investigaciones Científicas y Tecnológicas de la Universidad Católica*), que elaboró un diagnóstico completísimo de las emisiones y las medidas que debían adoptar las empresas para evitar superar los niveles de emisión.

En total en Huasco se emitían en 2013, 557 toneladas anuales de material particulado. La planta de Pellets podía emitir hasta 1.446 toneladas, anual, y Guacolda AES Gener hasta 919 toneladas, que suma el total de 2.362 toneladas de material particulado.

El esquema incluye además, los contaminantes NOx, SO2.

INGENIERÍA DICTUC

GreenLab UC, Gestión y Política Ambiental y Área Soluciones Ambientales

Tabla 3-6: Emisiones fuentes fijas de combustión (ton/año)

Empresa	Chimenea	2013					2020					2025				
		MP	MP10	MP2.5	NOx	SOx	MP	MP10	MP2.5	NOX	SOX	MP	MP10	MP2.5	NOx	SOx
CAP	2A	22	22	8	21	53	266	266	101	416	385	266	266	101	416	385
	2B	250	250	95	18	435	690	690	261	277	738	690	690	261	277	739
	3	0	0		0	0	490	490	185	381	578	490	490	185	381	578
CAP Total		**271**	**271**	**1.3**	**38**	**487**	**1,446**	**1,446**	**547**	**1,075**	**1,701**	**1,446**	**1,446**	**547**	**1,075**	**1,701**
Guacolda	U1_U2	149	149	57	4,251	17,866	318	318	120	4,558	3,646	318	318	120	4,558	3,646
	U3	95	95	36	1,796	816	213	213	81	2,406	1,923	213	213	81	2,406	1,923
	U4	42	42	16	232	6,353	243	243	92	285	1,933	243	243	92	285	1,933
	U5	0	0		0	0	146	146	55	285	966	146	146	55	285	966
Guacolda Total		**286**	**286**	**108**	**6,279**	**25,034**	**919**	**919**	**348**	**7,535**	**8,469**	**919**	**919**	**348**	**7,535**	**8,469**
Punta	PA1	0	0		0	0	317	317	120	2,337	2,337	317	317	120	2,337	2,337
Alcalde	PA2	0	0		0	0	0	0	0	0	0	317	317	120	2,337	2,337
Punta Alcalde Total		**0**	**0**		**0**	**0**	**317**	**317**	**120**	**2,337**	**2,337**	**633**	**633**	**240**	**4,673**	**4,673**
Total Fuentes Fijas Combustión		**557**	**557**	**211**	**6,317**	**25,522**	**2,681**	**2,681**	**1,015**	**10,946**	**12,507**	**2,998**	**2,998**	**1,134**	**13,282**	**14,843**

Fuente: Elaboración propia

NOTA: Las emisiones futuras (año 2025) fueron estimadas en base a factores de emisión de emisiones ambientalmente aprobadas según RCA Nº215/2010 del proyecto "Ampliación y Mejoras Operacionales en Planta de Pellets" (RCA N° 215/2010, 2010), RCA Nº44/2014 del proyecto "Adaptación de Unidades a la Nueva Norma de Emisión para Centrales Termoeléctricas" (COREMA III Región, 2014) y RCA Nº138/2012 "Central Termoeléctrica Punta Alcalde" (COREMA III Región, 2012))

Señaló que al iniciar la evaluación del plan de latencia –plan de prevención-, en septiembre de 2015 se consideró en el borrador del anteproyecto -de acuerdo con las emisiones del 2013- que la aplicación de las medidas para disminuir los niveles de emisión en un plazo de seis años permitía a CAP mantener igual el nivel de emisiones en los dos primeros años -272 toneladas por año- y, a contar del tercer año debía bajar a 139 toneladas al año. Para Guacolda se consideró que a contar del primer año si las cinco unidades operaban en forma simultánea por más de 500 horas en el año, su emisión máxima permitida sería de 328 toneladas al año. En caso de no cumplir esa exigencia, solo podían emitir 286 toneladas al año, es decir, el mismo valor consignado en el inventario de emisiones.

Posteriormente, en diciembre de 2015, todo cambió con la aprobación del anteproyecto del plan de prevención. Se determinó que el cumplimiento no era a seis años calendario, sino a 10 años al calendario siguiente a la entrada en vigencia del plan, es decir, se aumentó en un año el plazo para cumplir con la aplicación de las medidas.

Para CAP se determinó que debía cumplir con un valor máximo de emisión de 900 toneladas desde el primer año calendario siguiente por lo que desde el segundo año podían emitir 900 toneladas, y a contar del cuarto año –aunque dice tercer año calendario- la emisión máxima es de 341 toneladas, o sea, más de lo que mostraba el inventario pues este consignaban 271 para CAP y 286 para Guacolda. Por lo tanto, se acepta un valor de toneladas de emisión mayor. A la central Guacolda, de 286 toneladas consideradas en el borrador del anteproyecto se le aumentó el valor de emisión a 680 toneladas año.

En agosto de 2017 se aprobó el plan definitivo de latencia para Huasco, en el cual se dejó igual los siguientes años calendario y a la planta de Pellets se le mantuvo las 900 toneladas de emisión permitida, pero se aumentó el plazo en un año más, es decir, ya no al tercer año calendario, sino al cuarto año calendario lo que equivale en la práctica al quinto año, con una emisión máxima de 341 toneladas –cifra del anteproyecto- y a Guacolda se aumentó la emisión permitida de 680 a 730 toneladas anuales.

Agregó que otros impactos que no fueron considerados en la evaluación del plan de latencia es que no se evaluaron el SO_2 y el Nox, precursores del material particulado, ni tampoco se evaluó la composición química del contaminante material particulado como el arsénico, el vanadio, el mercurio, el níquel, el plomo y el cadmio.

Tampoco hubo medidas de mitigación para ninguno de los tres puertos de embarque de las empresas CAP y Guacolda, ni para el vertedero de cenizas de la empresa CAP de Guacolda, en que millones de toneladas de cenizas contaminan, sin considerar que hace 50 años se aprobó la termoeléctrica y los vientos que existen en la zona.

Reflexionó que fue contraproducente haber pasado años peleando por un plan de latencia, porque al final va a ser más nocivo para la zona. En razón de ello solicitó un nuevo plan de prevención o de descontaminación, y no de latencia si no que de saturación que se ajuste a las normas de contaminantes, porque aseguró conviven con una cámara de gas legalizada.

Hay que implementar en forma urgente nuevas normas, como la del níquel, vanadio, arsénico, entre otros gases, y metales pesados y activar la norma de

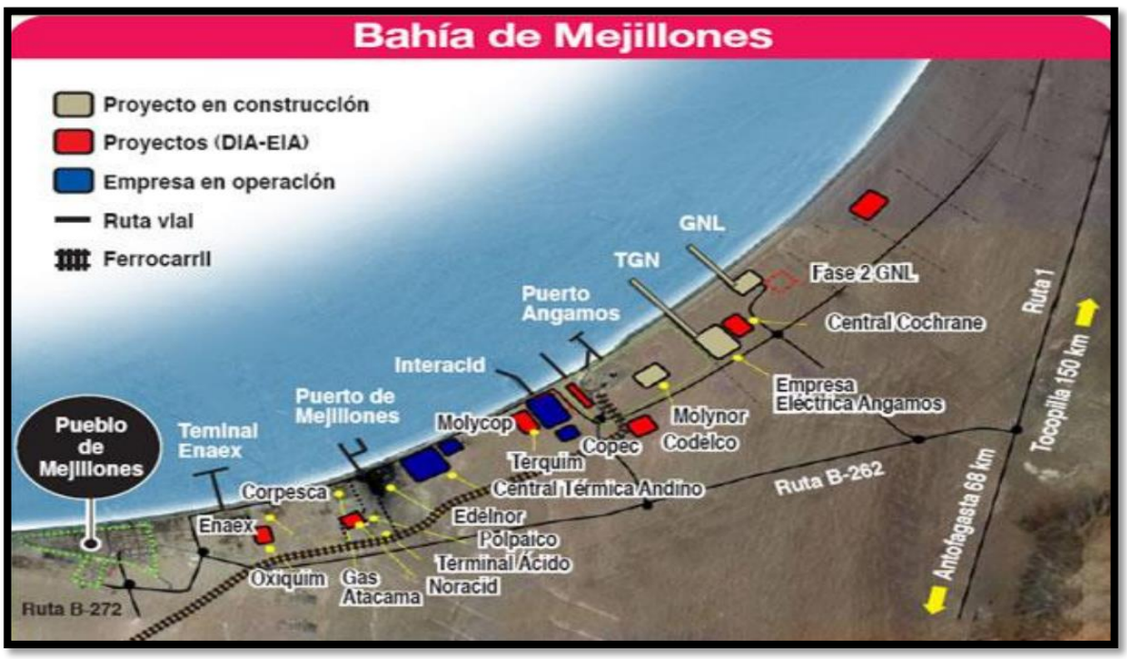
plomo. Las estaciones, de monitoreo, los informes y la fiscalización tienen que ser responsabilidad del Estado, porque no pueden estar en manos de las empresas, pues estas contratan empresas, hacen los monitoreos, envían los informes y se auto fiscalizan.

Finalizó, indicando que se deben establecer sanciones a las empresas en caso de no cumplir con las medidas propuestas en los planes de prevención y descontaminación.

48.- SEÑOR JONATHAN MENA, INTEGRANTE DE LA AGRUPACIÓN DESPIERTA MEJILLONES.

Señaló que Mejillones es una ciudad de 9.600 habitantes en la Región de Antofagasta. En esta localidad se han concentrado una gran cantidad de industrias ligadas al sector minero, entre ellas, cuatro centrales termoeléctricas a carbón con un total de seis unidades en funcionamiento.

Comentó que la primera empresa en instalarse en Mejillones fue Corpesca y Enaex hace 40 años y que actualmente hay empresas de almacenamiento de gas, el terminal TGN, Eléctrica Angamos; Central Cochrane; el puerto Angamos; empresas de molibdeno; una empresa refinadora; tanques de petróleo de Copec; Terquim; Molycop; Interacid; el puerto de Mejillones, con almacenamiento de plomo y zinc; Edelnor; Oxiquim, que genera energía a través de ácido; Gas Atacama; Noracid; Polpaico; Terminal de Ácido, y fue aprobada la termoeléctrica de ciclo combinado Kelar.



Sostuvo que un estudio de la Universidad de Antofagasta del año 2012, concluyó que en los sedimentos marinos del sector industrial se registran niveles de metales pesados (nique, cobre, zinc, cadmio, vanadio y plomo) que superan con creces la norma internacional. Además se encontró contaminación con metales pesados en varias especies de crustáceos y moluscos.

Enfatizó que la comunidad de Mejillones está preocupada por la contaminación industrial, por la declinación de los recursos marinos, los episodios de derrame de carbón y la mortandad de especies. Agregó que el año pasado se aprobaron más de cinco proyectos en Mejillones y ocho ya están en calificación. A pesar de todos los antecedentes de contaminación en la comuna, el gobierno sigue introduciendo proyectos contaminantes.

Informó que hace poco hubo derrame de petróleo en las playas del sector y que se acaba de aprobar la RCA a la empresa Engie para seguir operando por un año más en sus canteras de cenizas, que están a menos de 5 kilómetros de la comuna y cuando hay viento sur toda esa polución llega a Mejillones.

Indicó que durante las últimas dos décadas, la tasa de mortalidad ha aumentado principalmente por tumores y enfermedades al sistema circulatorio. Hay un consultorio muy básico y precario como para abordar estas enfermedades y otras porque también hay asociadas a problemas cognitivos y de aprendizaje, que realmente afectan mucho a la salud de los niños por estar expuesto por años a los metales pesados.

Explicó que cuentan con ocho unidades termoeléctricas a base de carbón y seis unidades más a base de ciclos combinado, lo que ha impactado en la salud de la población, especialmente las emisiones contaminantes de las termoeléctricas a carbón como el dióxido de carbono, material particulado, dióxido de azufre, óxidos de nitrógeno, metales pesados como el mercurio y un sinfín de minerales y químicos. Además, sostuvo que la absorción de agua que producen las termoeléctricas la generan por 78 kilómetros de largo y 10 kilómetros de profundidad, y por ello no existe biodiversidad.

Señaló que hay empresas que no son fiscalizadas porque el Ministerio del Medio Ambiente tiene muy pocos recursos y en general, las sanciones o multas no son un aliciente para contribuir a la mejora de la calidad de vida de las comunas.

La región es primordialmente minera, por lo que las localidades de las nueve comunas de la región de Antofagasta no cuentan con controles ni monitoreos constantes respecto de la situación medioambiental.

Apuntó que el carbón cae a las playas hace más de 25 años, al igual que otros minerales. Agregó que un informe dio cuenta de la presencia de 14 metales pesados en las techumbres del establecimiento educacional, con altas concentraciones de arsénico, talio, plomo, plata, magnesio, hierro, cobre, cadmio, mercurio, zinc, molibdeno y cobre. Es decir, todo lo que extrae la minería y transporta a los puertos se concentra en los establecimientos y en las comunas.

Concluyó señalando que esperan que haya justicia para las comunidades y se adopten las medidas para mejorar a corto plazo las normativas medioambientales; que no se sigan aceptando proyectos contaminantes y que disminuyan las enfermedades, para que mejore la calidad de vida y la salud de la personas. Sostuvo que el estado debe responsabilizarse por los costos que ha significado años de producción a las empresas.

49.- FERNANDO SAN ROMÁN, EXCALDE E INTEGRANTE DE LA ORGANIZACIÓN TOCOPILLA VUELVE.

Relató que como alcalde de la comuna, entre 2012 y 2016, llevaron adelante ciertas medidas a través del equipo municipal, con todas las precariedades que significa un municipio que no cuenta con todas las facultades legales, ni tampoco económicas.

Señaló que en 2003, Tocopilla, por haberse superado la norma anual de manera consecutiva durante tres años, ya se encontraba en una situación de zona saturada. En el año 2004 se inician las primeras gestiones para el procedimiento de declararla zona saturada y también se inician gestiones para realizar un estudio por parte del Dictuc, financiado por el Estado, cuyo resultados fueron entregados en el año 2015 y concluyeron que las fuentes emisoras contaminantes en Tocopilla eran de responsabilidad de dos empresas termoeléctricas, AES Gener y Electroandina, que actualmente se llama Engie. El año 2006, la Comisión Regional de Medio Ambiente, Corema, declaró a Tocopilla como zona saturada y en el año 2007 se dicta el decreto correspondiente, y recién en el año 2010 comienza a regir el plan de descontaminación que actualmente sigue vigente.

En síntesis, afirmó que en todo este proceso queda demostrado la burocracia y lentitud estatal, pasaron todos estos años en tramitación mientras las ciudades saturadas siguen con contaminación sin que se inicien y adopten las medidas concretas para resguardar la salud de la población.

Indicó que en 2014 iniciaron una batalla legal, junto a otros municipios de Chile y organizaciones, porque en diciembre de 2013 se dictó un decreto que derogaba la norma anual de material particulado. Dicho decreto, a juicio del municipio en la época, y de otras organizaciones sociales e instituciones, significaba darle “manga ancha” a las termoeléctricas y poner en riesgo los planes de descontaminación vigentes. Recurrieron al tribunal ambiental, donde se ganó la batalla judicial, pero el Consejo de Defensa del Estado presentó un recurso de casación para defender el decreto que derogaba la norma anual. Finalmente, se llegó a la Corte Suprema, que en 2015 dictó un fallo definitivo por el cual se deroga el decreto y mantiene la norma vigente anteriormente.

Recordó que en 2014 el entonces alcalde de Puchuncaví, Hugo Rojas, invitó a varios municipios a conformar la primera organización “Unión de Municipios en Zonas de Sacrificio”, con el objeto de agrupar y organizar a aquellas municipalidades que tenían termoeléctricas y graves problemas de contaminación, las cuales eran denominadas zonas de sacrificio y se logró generar una agenda de trabajo, que se fue diluyendo en el tiempo porque algunos alcaldes no siguieron participando y el tema dejó de estar en la palestra.

Apuntó que en Tocopilla existen actualmente dos empresas termoeléctricas: AES Gener con dos unidades y Engie que tiene cuatro unidades. Engie anunció que el próximo año se cerrarán dos unidades, que son las más antiguas de Tocopilla y de Chile, pues tienen más de 40 años de funcionamiento, y que en 2020 cerraría las otras dos. Es decir, Engie no seguirá contando con unidades termoeléctricas en un plazo de dos a tres años en la comuna de Tocopilla.

Declaró que si bien se reconoce que las empresas termoeléctricas generan empleos, en la población total de una comuna como Tocopilla, que tiene

cerca de 30.000 habitantes, el impacto es menor en relación con la cantidad de habitantes. Por ejemplo, como consecuencia del cierre de las dos unidades termoeléctricas de Engie el próximo año, se está hablando de aproximadamente veinte puestos de empleo. Sin embargo, muchas veces se les decía que se estaba hablando de 1.000 o 2.000 puestos de trabajo, lo que no corresponde a la realidad. Las mismas empresas, en las reuniones que han pedido con el Ministerio de Energía, han transparentado esos datos y han señalado cuáles son los puestos de empleo que se generan.

Destacó que el gran desafío de Tocopilla y de la otras comunas de Chile sometidas históricamente a esta contaminación consiste en superar la dependencia de empresas termoeléctricas contaminantes y pasar a otro tipo de generación de empleo y de energía, aprovechando, por ejemplo, las bondades para producir energía solar que se tiene en el norte, como producto de la alta radiación, las que no han sido aprovechadas ni explotadas del todo.

Sobre las estaciones de monitoreo precisó que todos los datos que se tuvieron a la vista en Tocopilla para tomar medidas, emprender acciones y plantear temas ambientales fueron otorgados por los monitoreos que hacen las mismas empresas, mediante estaciones que son administradas y operadas por ellas misma, sin que exista un mínimo de transparencia ni objetividad, como podría haber en una estación monitora manejada por el Estado.

Informó que Tocopilla hasta el año 2016 también tenían botaderos de cenizas, donde las empresas industriales dejaban sus desechos a 400 metros de una población donde viven alrededor de 600 familias tocopillanas, sin embargo pese a que fueron cerrados las cenizas quedaron y se aplicó un tratamiento que consistió en hacer un relleno con una capa de tierra, pero no existe un plan de cierre ni otras medidas, y en el año 2015, cuando en Tocopilla se produjo un aluvión, uno de los aludes pasó sobre las cenizas y esos desechos escurrieron hasta el mar. Luego de eso Directemar tomó muestras y determinó que había presencia de contaminantes en el borde costero de Tocopilla. Se hicieron denuncias a la Superintendencia del Medio Ambiente, pero nunca hubo un proceso sancionatorio.

Respecto de las normativas explicó que, efectivamente, con un plan de descontaminación tienden a bajar la contaminación, sin embargo la atención se debe poner en la normativa ambiental vigente que es insuficiente, a juicio de muchas de especialistas, organizaciones e instituciones. En efecto, si se compara las emisiones que hay actualmente en Tocopilla, es posible que estén en el límite de la norma chilena, pero si las comparamos con las normas de la OMS, aún se está muy lejos.

Expresó que plantea esto porque es necesario que se generen cambios en la legislación y también que las comunas que han sido sometidas históricamente a esos graves efectos de la contaminación tengan apoyo del Estado y de las empresas privadas para generar planes de desarrollo económico que permitan cambiar la matriz termoeléctrica y pasar a otro tipo de generación y crear un plan de desarrollo económico sin dejar abandonadas a esas comunas.

Sostuvo que las zonas de sacrificio tiene un factor común: son comunas pobres, pequeñas, a las que se ha excluido del tejido social, porque las empresas hacen aportes a las organizaciones, y muchas veces incluso cooptando a algunas organizaciones, que han partido con un discurso muy crítico, pero luego, en el camino,

al recibir financiamiento de esas empresas, han terminado disminuyendo su discurso más duro y muchas veces dejando de criticar la contaminación.

Estimó que a pesar de los esfuerzos que se hizo desde la Municipalidad de Tocopilla para enfrentar la contaminación y tomar algunas medidas, faltan facultades y recursos para los municipios. Por ejemplo, nunca se pudo contar con los recursos para elaborar un estudio destinado a confirmar la causalidad en enfermedades como cáncer y afecciones respiratorias, que son muy comunes en Tocopilla, ni tampoco se tuvo recursos ni el apoyo del Estado para realizar exámenes a la población y un estudio epidemiológico.

Fue enfático al señalar que es necesario que haya más facultades y recursos para la Superintendencia del Medio Ambiente, porque muchas veces se hacen denuncias pero no hay funcionarios para fiscalizar. Es algo bastante lamentable y que, obviamente, se repite en otras comunas subrayó.

50.- SEÑOR ERIC BAHAMONDES, SECRETARIO DEL MOVIMIENTO ARRIBA TOCOPILLA.

Comentó que en Tocopilla hay una termoeléctrica que fue construida en 1914, por la empresa Chile Exploration Company, para suministrar energía al mineral de Chuquicamata. En 1971 fue nacionalizada y pasó a manos del Estado chileno, y posteriormente a Codelco, como parte de la División Chuquicamata. Este tejido histórico ha contribuido a la instalación de estas empresas pero también hay personas que por generaciones han trabajado en ella.

Tocopilla cuenta con 7 Centrales, la termoeléctrica de AES Gener. AES Gener que cuenta con dos unidades y Engie con cinco unidades siendo las más antiguas del país que funcionan desde 1967, es decir, llevan más de 40 años en funcionamiento.

A pesar de que existe la noción de la contaminación y del daño medio ambiental y es tangible en la población las enfermedades provocadas por las emisiones de partículas contaminantes de las empresas termoeléctricas, el miedo a que no exista un plan alternativo de producción que cambie la matriz productiva de Tocopilla lleva a que los tocopillanos defiendan la instalación o la permanencia de las termoeléctricas.

Enfatizó que es muy triste ver que en las escuelas técnicas se prepara a los estudiantes para ir a trabajar en una termoeléctrica, a pesar de que hoy una empresa de ese tipo no genera más de doscientos o trescientos puestos de trabajo.

Finalizó diciendo que en 2007, Tocopilla fue decretada como zona saturada, cuyo decreto fue firmado en 2010, pero hasta el día de hoy no se ha llevado a cabo ese plan.

51.- ELIANA OLMOS, ALCALDESA DE LA COMUNA DE PUCHUNCAVÍ.

Por acuerdo de la Comisión, le fue remitido un cuestionario escrito, cuyas preguntas y respuestas se consignan a continuación:

1.- Actualmente el PREMVAL autoriza la disposición de suelo para instalar industria peligrosa en la zona de Quintero/Puchuncaví.

a) ¿Considera adecuado permitir que se siga instalando industria en su comuna?

He manifestado públicamente mi rechazo respecto a la llegada de nuevas industrias molestas y peligrosas a la comuna de Puchuncaví ya que es una zona que ha sufrido por más de 50 años, afectando la salud de las personas, el medioambiente y la calidad de vida de nuestros vecinos, por lo que a nuestro territorio no deben seguir llegando nuevos proyectos de este tipo. Como comuna hemos entregado lo suficiente, nos hemos sacrificado y puesto al servicio del país por muchos años, sin tener una retribución o desarrollo acorde a lo que hemos entregado, así que no podemos seguir aceptando la llegada de nuevos proyectos contaminantes.

b) La Ley General de Urbanismo y Construcción (LGUC) faculta a dos o más municipios para solicitar la modificación del PREMVAL ¿está dispuesta a tomar esta medida?

Como municipio, y en relación a nuestro interés de que no lleguen nuevas empresas contaminantes a nuestra comuna, solicitamos formalmente el día 5 de septiembre, a través de una carta conjunta con el municipio de Quintero, dirigida al Seremi de Vivienda y Urbanismo, la modificación del PREMVAL, toda vez que este instrumento considera una importante cantidad de hectáreas de terreno en nuestra comuna, que están disponibles para la llegada de empresas molestas y peligrosas. Por lo mismo, realizamos esta solicitud, esperando que sea acogida y se hagan todos los trámites necesarios para que se cumpla y así aseguremos a nuestros vecinos que no seguiremos siendo perjudicados y afectados con la llegada de empresas contaminantes.

2.- ¿Cuántos trabajadores del cordón industrial, considerando contratistas y de planta, residen en la comuna de Puchuncaví y Quintero? ¿Cuál sería el impacto de detener la producción sea en forma temporal o definitiva? Análisis y propuesta

En estos momentos no se cuenta con un catastro exacto de personas que desempeñan labores en las empresas del complejo industrial, ya sean contratadas, de planta o de alguna empresa contratista, que residen en las comunas en comento. Pero sin duda el número no es menor, sin contar con los servicios que las comunas prestan a los trabajadores del sector industrial, ya sea alimentación y/o alojamiento, entre otras.

Me ha tocado escuchar en diversas ocasiones que la única solución es cerrar el parque industrial, en un análisis muy superficial del efecto que esto puede tener para la comuna.

Puede gustarnos o no, pero hay mucha gente que depende de las empresas, ya sea de manera directo o indirecta, por lo que el cierre de todas las empresas requiere un análisis más profundo, más serio, para determinar quién se hará cargo del problema social que se nos originaría, quien asumirá la atención de las necesidades que tendrán las familias que queden sin su fuente laboral, las que aseguro llegarán al municipio por ayuda.

Lo que si yo creo y soy una convencida, que debemos aprender a convivir, y sobre todo, regular el funcionamiento del parque industrial, porque acá se evidencia un desequilibrio porque las empresas han crecido con total libertad y hoy nos encontramos con un gran problema. Hoy lo que corresponde es regular, ordenar, de

manera que se cumplan con las nuevas normas, con los parámetros más exigentes, pero no seguir funcionando como viene siendo hasta el día de hoy, con libertad absoluta para las industrias y problemas para la comunidad.

Respecto del cierre, yo pediría una discusión un poquito más profunda, no quedándonos sólo en el hecho efectista, sino que en las consecuencias de la acción de cerrar, porque después la atención se trasladará a otros temas y el municipio seguirá quedando no con un problema medioambiental, sino que un problema social, del cual no podemos hacernos cargo.

Pero quiero dejar claro que si hay empresas que no están en condiciones de cumplir con la norma debe cerrar, pero cuidado cuando se toman casi como lema de campaña el cierre de las industrias, porque se puede generar otro problema del que el municipio no puede hacerse cargo.

3.- Dentro de la municipalidad ¿existe alguna unidad de control medioambiental?, ¿existen protocolos o planes de emergencia frente a episodios de contaminación?, ¿se ha conversado con el gobierno central la factibilidad de traspasar recursos para llevar adelante una institucionalidad ambiental local y normas o mecanismos que permitan actuar adecuadamente frente a una emergencia?

Esta emergencia ha dejado en evidencia que los municipios no tenemos las suficientes herramientas, ni técnicas ni administrativas, para enfrentar emergencias de este tipo, dependemos de otros organismos que cumplan con esta tarea como es bomberos o esperar a que se hagan presente organismos como el Servicio de Salud, Superintendencia de Medioambiente, quedando siempre a la disposición y disponibilidad de estas instancias.

Nosotros como municipio tenemos un protocolo ante el cual reaccionamos para enfrentar estas emergencias y que dice relación con que la emergencia es informada al Encargado Comunal de Emergencia y él informa a su vez a ONEMI y esa información posteriormente es transmitida a los servicios públicos con competencia en el tema. Además se provoca una activación de toda la red comunal (salud, bomberos) de manera de estar atentos al desarrollo de la situación.

En base a la última emergencia, ahora se agregó la existencia de las zonas seguras, que son espacios que cuentan con purificadores de aire, y que es donde se concentrarían los alumnos en el caso de un episodio de contaminación.

Respecto a la necesidad de traspaso de recursos para fortalecer estas unidades claves y fundamentales para los municipios, quiero decir que es una situación que se ha manifestado en reiteradas ocasiones, donde no tan sólo el área medioambiental requiere un fortalecimiento, sino que diversas áreas municipales, las que no han podido crecer debido a que no se han ampliado las plantas municipales y nos encontramos con situaciones donde debemos contratar a honorarios a muchos profesionales o con sueldos que no permiten mantenerlos trabajando en el municipio, pues en la parte privada ganan mucho más dinero y prefieren irse. Lo anterior lo he manifestado en reuniones con diversas autoridades, a quienes planteamos esta problemática.

4) Aunque la legislación no contempla la obligación de que las consultas ciudadanas sean vinculantes, los alcaldes tienen la facultad de que si lo sean, tal

como lo han hecho los alcaldes de Valparaíso y Las Condes. Dada la seriedad del asunto y que éste se refiere a la dignidad de los habitantes de las comunas:

a) ¿No les parece adecuado aprovechar las instancias de consultas ciudadanas para hacer respetar lo que la mayoría efectivamente quiere para su comuna?

Entendemos que efectivamente en las participaciones ciudadanas la idea es que consideren las observaciones que los asistentes puedan hacer, quienes plantean sus puntos de vista, preocupaciones o visión respecto a un proyecto determinado. Quizás lo que se debiera buscar, es cómo mejorar el propio sistema de participación, para que sea realmente "participativa", "representativa" y principalmente VINCULANTE. De manera tal, que la comunidad se sienta CONSIDERADA en todo el contexto de la palabra, y no solamente siendo parte de un trámite para cumplir con algún ítem del proyecto en cuestión.

b) ¿Estarían dispuestos a comprometerse con la ciudadanía en este sentido y sumarse a la demanda que exigen?

Primero que todo quisiera decir y manifestar que acá la comunidad y lo que piensan los alcaldes no están en veredas contrarias, lo que la gente pide y siente, es lo mismo que las autoridades pensamos, por lo que no es bueno crear una sensación, que aquello que la comunidad manifiesta no tiene eco en sus autoridades. Lo que ocurre es que como autoridades trabajamos en ámbitos distintos. Muchas de las gestiones que hacemos la gente no las ve, pero los alcaldes de Puchuncaví y Quintero, están luchando por avanzar en soluciones reales a los problemas de contaminación que existen en las comunas, tal como lo quiere la gente, por lo que pedirnos que nos comprometamos con las demandas de la comunidad está de más.

Nadie debe contarme cómo es el problema de contaminación en nuestro territorio, lo conozco porque he vivido toda mi vida en la comuna de Puchuncaví, acá la solución debe venir desde el Estado de Chile, los municipios tienen muy pocas atribuciones legales o administrativas.

Como autoridades comunales, por años hemos trabajado fuertemente en abordar el tema de la contaminación, lo que pasa que nunca existió un respaldo político transversal como el que se está teniendo ahora, donde diferentes sectores políticos, parlamentarios y autoridades regionales han puesto su atención y foco en nuestras comunas, hoy se han generado condiciones especiales para poder apuntar a soluciones más reales y concretas.

Por lo mismo, si a algo hay que comprometerse como Alcaldes, nos podemos comprometer a continuar desarrollando nuestro trabajo, que lo venimos haciendo hace mucho rato. Lo interesante sería que todos aquellos que hoy nos apoyan se comprometan con la comunidad a seguir haciéndolo, y no dejarnos una vez que este tema deje de estar en los medios de comunicación.

5) Teniendo en cuenta que en Chile existe un debate en torno a la normativa de calidad y emisión de contaminantes.

a) ¿Cuál es su opinión acerca de las normas europeas versus las normas que define la OMS para reglamentar las emisiones de gases tóxicos?

Claramente nosotros como país debemos apuntar a normas mucho más estrictas y restrictivas que las existentes. Nosotros estamos mirando a la normativa de la Unión Europea que es mucho más exigente. Ahora se debe dejar en claro la OMS no tiene norma, ellos sugieren a los países parámetros para aplicar en los respectivos territorios.

Lo importante de todo esto es que mejoremos lo existente y que las normas nos aseguren que tenemos un aire respirable y un ambiente que no está afectando la salud de las personas. Ahora lo que se debe tener claro es que se debe considerar la realidad de cada país, pero debemos acercarnos a normas como las de la OMS que aseguran la salud de los habitantes de los territorios.

b) ¿Considera necesario avanzar hacia una homologación de normas internacionales? ¿A cuáles?

Absolutamente se hace necesario y fundamental poder mejorar la situación actual, se debe homologar nuestra normativa a países que van mucho más avanzados que nosotros y quienes tienen una realidad similar, vale decir cuentan con industrias y han sabido trabajar los temas medioambientales, asegurando una calidad de vida para los habitantes de nuestro territorio.

Tenemos que ser capaces de mirar nuestra realidad y aplicar la normativa suficiente para que las personas no sufran por el accionar de un complejo industrial como el que tenemos en Puchuncaví.

6) ¿Cómo evalúan la actuación del gobierno en la emergencia y la coordinación que ha existido entre los diversos servicios públicos?

Siento que ha habido aciertos y algunas cosas que se podrían haber hecho mejor, sin embargo se debe destacar que las autoridades vinieron y se instalaron en el territorio, lo que permitió abordar la emergencia de una manera mejor, con situaciones que pudimos ir planteando de manera mucho más cercana e inmediata, a que si los comités operativos de emergencia (COE) se hubieran realizado en Valparaíso.

Claramente nos vimos enfrentados a situaciones nuevas, emergencias que provocaron un gigantesco problema, con miles de personas intoxicadas, por lo que a ratos diversas instancias se vieron sobrepasadas.

Creo que dentro de todo, fue fundamental que se haya incluido a los municipios dentro de cómo abordar la emergencia, más allá de que hay organismos que tenían competencia exclusiva en ciertos temas, pero la participación de los municipios permitió darle el peso local a la solución al problema.

7) ¿En qué estado se encuentra la petición que formulara el Diputado Diego Ibáñez y el Senador Juan Ignacio Latorre acerca de hacer uso de la facultad del artículo 160 de LGUC? ¿Cuál es el motivo por el que aún no se ejerce la posibilidad que otorga esa norma?

La petición que formulara el Diputado Diego Ibáñez Cotroneo y el Senador Juan Ignacio Latorre Riveros, se encuentra en el estado informado en el Oficio N° 982 y N° 981, ambos de fecha 20 de septiembre de 2018, dirigido a las autoridades nombradas, respectivamente.

52.-SEÑOR OSCAR SUMONTE, ALCALDE DE LA COMUNA DE CONCON.

Por acuerdo de la Comisión, le fue remitido un cuestionario escrito, cuyas preguntas y respuestas se consignan a continuación:

1) El PREMVAL autoriza la disposición de suelo para instalar industria peligrosa en la zona de Quintero/Puchuncavi.

El Seccional Enap, el cual se encuentra vigente, corresponde a una zonificación del PREMVAL que permite la instalación de Industria Peligrosa, y mantuvo las antiguas disposiciones del PIV para ese territorio (E7A). De lo anterior se desprende que no sólo las comunas de Quintero y Puchuncaví permiten este tipo de industrias, lo cual hoy día faculta a ENAP para que desarrolle proyectos termoeléctricos.

a) ¿Considera adecuado permitir que se siga instalando industria en su comuna?

La comuna de Concón dispone de un barrio industrial (ZPM) que permite el desarrollo de actividades productivas molestas (INDUSTRIA NO PELIGROSA). Por lo tanto, no existe incompatibilidad territorial, permitiendo que este tipo de industria sea parte del motor de desarrollo de una comuna, atrayendo viajes, generando movilidad, moviendo la economía, etc. Es prudente aclarar que La comunidad se ha manifestado en contra de la industria peligrosa (E7A), la normativa de la zona E7A, o del actual seccional Enap, no distingue entre una bodegas de almacenamiento de sustancias peligrosas, volátiles y explosivas, al lado de plantas de gas y de refinación de hidrocarburos, junto a fuentes de energía en base a hidrocarburo o gas, que generan contaminación particulada en una zona declarada saturada y que, además, utiliza los pocos recursos naturales disponibles en el territorio (agua del Aconcagua), etc.

Es la industria peligrosa la que preocupa y que ha provocado el malestar de la comunidad. El seccional Enap se ubica entre las dos zonas urbanas de la comuna, el Concón viejo o poniente y Concón oriente (ex zonas de extensión urbana del PREMVAL) que es hacia donde crece la comuna. Ese malestar se incrementa más cuando se permiten seguir instalando proyectos de industriales peligrosos en un territorio que aún no soluciona los problemas medioambientales que existen actualmente en el sector.

b) La actual Ley General de Urbanismo y Construcción (LGUC) faculta a dos o más municipalidades para solicitar la modificación del PREMVAL. ¿Está dispuesto a tomar esta medida?

La decisión para solicitar una modificación a un Instrumento territorial de planificación (ITP) es política. Desde el ámbito técnico, y según la situación que actualmente enfrenta el municipio y que tiene relación con las industrias peligrosas emplazadas en la comuna y que generan profundo malestar en la comunidad, es posible establecer que la autoridad municipal y con el apoyo de la mayoría del concejo municipal pueden estar dispuestos a tomar dicha medida.

2) ¿Cuántos trabajadores del cordón industrial, considerando contratistas y de planta, residen en la comuna de Puchuncaví y Quintero? ¿Cuál sería el impacto de detener la producción, sea en forma temporal o definitiva? Análisis y propuestas.

El municipio de Concón no cuenta con dicha información por cuanto escapa a nuestro ámbito administrativo.

3) Dentro de la municipalidad, ¿exististe alguna unidad de control medio ambiental?, ¿existen protocolos o planes de emergencia frente a episodios de contaminación?, ¿se ha conversado con el gobierno central la factibilidad de traspasar recursos para llevar adelante una institucionalidad ambiental local y normas o mecanismos que permitan actuar adecuadamente frente a la emergencia?

El municipio de Concón cuenta con una Dirección de Emergencia asociado a Fiscalizaciones, la cual está principalmente orientada a dar respuesta a accidentes naturales o la asociación de estos con accidentes naturales y tecnológicos.

Respecto de la problemática ambiental, el municipio cuenta con una Oficina de Medio Ambiente -perteneciente a la "Dirección de Tránsito y Operaciones"- y se encuentra conformada por dos profesionales contratados y dos consultores externos, estos últimos cumplen una función de asesoramiento técnico en los temas ambientales de distinta índole. Este equipo ha permitido enfrentar distintas situaciones ambientales relacionadas con proyectos que se tramitan en el SEIA como a la activa participación respecto al desarrollo del PDA, formulación de ordenanzas, sobre todo aquellas relacionadas con áreas protegidas y a instancias de mediación ante la Participación Ciudadana.

Es menester indicar que durante los tres últimos años el municipio de Concón ha estado trabajando en el desarrollo de protocolos que permitan involucrar al municipio dentro de los planes de emergencia de las empresas emplazadas en la comuna, lo cual está considerado dentro del Plan Nacional de Seguridad Química del MMA. Todo lo anterior involucra un trabajo en conjunto con las respectivas empresas.

4) Aunque la legislación actual no contempla la obligación de que las consultas ciudadanas sean vinculantes, los alcaldes tienen la facultad de que, si lo sean, tal como lo han hecho los alcaldes de Valparaíso y de Las Condes. Dada la seriedad del asunto y que este se refiere a la dignidad de los habitantes de las comunas:

a) ¿No les parece adecuado aprovechar las instancias de consultas ciudadanas para hacer respetar lo que la mayoría efectivamente quiera para su comuna?

El municipio de Concón ha trabajado fuertemente en incentivar la PAC, sobre todo en lo que respecta a proyectos sometidos al SEIA de manera que la ciudadanía conozca las alternativas de que dispone al obtener la "legitimación activa". En tal sentido, la actual administración ha apoyado, financiado y se ha hecho parte de procesos judiciales cuando los derechos fundamentales de los vecinos de la comuna se ven vulnerados, ejemplo de lo anterior fue el proceso judicial que se llevó acabo en la Corte de Apelaciones de Valparaíso contra al Rex 264/2013 del SEA región de Valparaíso respecto de la "Modificación Central Combinada ERA" de ENAP.

El apoyo del municipio hacia la comunidad ha estado centrado en traspasar información de carácter técnico apoyada en estudios científicos de manera de tener una ciudadanía informada responsablemente sobre sus derechos y demandas.

b) ¿Estarían dispuestos a comprometerse con la ciudadanía en este sentido y sumarse a las demandas que exigen?

El municipio de Cancón apoya toda demanda colectiva que tenga sustento técnico y legal. Esto incluye análisis de riesgo o una evaluación de riesgo que permita establecer el origen de los agentes contaminantes, condiciones de exposición única o repetida, rutas ambientales, vías de ingreso a la población, concentraciones letales en mamíferos y en ecosistemas. Esto con el objeto de evitar acciones que desprestigien la acción gubernamental y la pérdida de credibilidad de quien apoye estas demandas.

5) Teniendo en cuenta que en Chile existe un debate en torno a la normativa de calidad y emisión de contaminantes:

a) ¿Cuál es su opinión acerca de las normas europeas versus las nomas que define la OMS para reglamentar las emisiones de gases tóxicos?

Las normas internacionales son buenos referentes respecto a los criterios utilizados para su promulgación. Sin embargo, la elaboración de ellas y que define objetivos, metas, seguimiento y alcance debe ser desarrollada localmente considerando el contexto biogeográfico. La implementación de normas internacionales que no consideren la realidad geográfica del territorio y que pretenden normarlo, puede transformarse en una iniciativa que genere externalidades negativas lo cual incrementaría el riesgo pre-existente.

Por lo tanto, se requiere de la implementación de consideraciones técnicas, científicas y legales que hagan comparables las normas internacionales con las nacionales. También se hace necesario que las empresas implementen unidades técnicas de investigación y desarrollo, para efectuar mejoras continuas en materia de seguridad química de manera de actuar preventivamente y no reactivamente.

b) ¿Considera que es necesario avanzar hacia una homologación de normas internacionales? ¿A cuáles?

Previamente debe efectuarse un levantamiento de la información técnica y fundamentos como se señaló en el punto anterior. Comparar las normas con países desarrollados con realidades similares, a modo de ejemplo metales como arsénico (As) y plomo (Pb) en suelos comparados con países de la misma realidad biogeográfica como Nueva Zelanda, Australia y Europa. A su vez las recomendaciones regulatorias de agencias como EPA, ECHA, OMS, OIT por señalar algunas.

6) ¿Cómo evalúan la actuación del gobierno en la emergencia y la coordinación que ha existido entre los diversos servicios públicos?

El municipio de Concón evalúa positivamente el accionar del actual gobierno en lo que respecta a la pronta implementación del PDA producto de la emergencia ambiental ocurrida en Quintero y Puchuncaví durante la segunda mitad del año anterior. Esto se sustenta en que el actual PDA tiene una alta probabilidad de alcanzar el objetivo propuesto, donde los antecedentes técnicos aportados por el municipio de Concón, como la incorporación de diversos aspectos nacidos en el seno

de la PAC y la alta exigencia interpuesta a las megas fuentes fueron debidamente considerados.

El municipio de Concón sólo lamenta que el Ministerio del Medio Ambiente no haya enviado el PDA a los municipios antes del su ingreso a la Contraloría General de la República, situación que estaba comprometida la actual ministra.

El accionar el actual gobierno -en lo que respecta al PDA- refleja por primera vez una organización del aparato estatal en esta área, capaz de liderar los temas ambientales y de efectuar las medidas de monitoreo para establecer origen y circunstancias, similar a las exigencias hechas por la EPA y ECHA.

53.-SEÑOR MAURICIO CARRASCO PARDO, ALCALDE DE LA COMUNA DE QUINTERO.

Por acuerdo de la Comisión, le fue remitido un cuestionario escrito, cuyas preguntas y respuestas se consignan a continuación:

1.- El PREMVAL autoriza la disposición de suelo para instalar industria peligrosa en la Zona de Quintero -Puchuncaví.

a) ¿Considera adecuado permitir que siga instalando industria en su comuna?

Esta Alcaldía no considera ni considerará la instalación de nuevas industrias peligrosas en todo el territorio.

b) La actual Ley General de Urbanismo y Construcción (LGUC) faculta a dos o más Municipalidades para solicitar la modificación del PREMVAL. ¿Está dispuesto a tomar esta medida?
Si estaría dispuesto a solicitarlo dentro de mis facultades.

2) ¿Cuántos trabajadores del cordón industrial. Considerando contratistas y de planta residen en la comuna de Puchuncaví y Quintero? ¿Cuál sería el impacto de detener la producción sea en forma temporal o definitiva? Análisis y Propuesta.

El catastro de esa información no se encuentra en esta Alcaldía, sin embargo, cualquier detención de la producción cualquiera sea su forma impactaría no solo a nivel comunal, sino también a nivel regional, incrementando la cesantía.

3) Dentro de la Municipalidad. ¿Existe alguna unidad de control medio ambiental? ¿Existen protocolos o planes de emergencia frente a episodios de contaminación? ¿Se ha conversado con el gobierno central la factibilidad de traspasar recursos para llevar adelante una institucionalidad ambiental local y normas o mecanismos que permitan actuar adecuadamente frente a la emergencia?

Dentro de la Municipalidad existe una Unidad de Medio Ambiente, que desde este año pasa a ser parte del Departamento de Aseo. Ornato y Medio Ambiente.
No existen Protocolos o planes de emergencia frente a episodios de contaminación, ya que estos no debiesen ocurrir.

Si, se ha conversado

4) Aunque la legislación actual no contempla la obligación de que las consultas ciudadanas sean vinculantes, los alcaldes tienen la facultad de que sí lo sean, tal como lo han hecho los Alcaldes de Valparaíso y de las Condes.

a) ¿No les parece adecuado aprovechar las instancias de consulta ciudadana para hacer respetar lo que la mayoría efectivamente quiera para su comuna?

Sí, siempre se han recibido las opiniones y sugerencia de la ciudadanía.

b) ¿Estarían dispuestos a comprometerse con la ciudadanía en este sentido y sumarse a las demandas que exigen?

Este Municipio siempre se ha sumado a la preocupación y demandas de la ciudadanía, toda vez que se han visto afectados los derechos para vivir en un lugar libre de contaminación, como por ejemplo las acciones legales en casos de derrames, de contaminación entre otros.

5) Teniendo en cuenta que en Chile existe un debate en torno a la normativa de calidad y emisión de contaminantes:

a) ¿Cuál es su opinión acerca de las normas europeas versus las normas que define la OMS para reglamentar las emisiones de gases tóxicos?

Primero que todo la OMS no cuenta con normativa sino que ellos entregan recomendaciones de las concentraciones de contaminantes que puede permitir una persona y todas las normas chilenas debiesen ser como la normativa europea.

b) ¿Considera que es necesario avanzar hacia una homologación de normas internacionales? ¿A cuáles?

Si, a la europea

6 ¿Cómo evalúa la actuación del gobierno en la emergencia y la coordinación que ha existido entre los diversos servicios públicos?

Durante la emergencia bastante más coordinado que post emergencia.

IV.-INFORMACIÓN SOLICITADA.

La Comisión acordó el despacho de diversos oficios sobre materias relacionadas con su investigación, los que se consideran con indicación de si hubo o no respuesta, que se adjuntan en las actas respectivas y se anexan al presente informe:

Asimismo acordó agrupar los oficios según:
Si han sido contestados dentro del plazo de 30 días
Si han excedido el plazo de 30 días.
Aquellos respecto de los cuales a la fecha de este informe no han recibido respuesta.

OFICIOS CONTESTADOS DENTRO DEL PLAZO DE 30 DÍAS.

Oficio N° 09

Fecha	28-09-2018
Destinatario	**Ministra del Medio Ambiente, señora Carolina Schmidt.**
Materia:	Que informe las medidas realizadas por esta institución, desde el 21 de agosto hasta la fecha, con motivo de lo ocurrido en Quintero y Puchuncaví.
Respuesta:	Recibida el 26 de octubre mediante el cual informó las medidas adoptadas por el Ministerio en relación al problema ambiental que afecta a Quintero y Puchuncaví desde el 21 de agosto hasta el 25 de octubre, fecha del informe.

Oficio N° 10

Fecha	28-09-2018
Destinatario	**Superintendente del Medio Ambiente, señor Cristian Franz.**
Materia:	Que informe sobre todas las medidas realizadas por esta institución, desde el 21 de agosto hasta la fecha, con motivo de lo ocurrido en Quintero y Puchuncaví.
Respuesta:	Recibida el 26 de octubre.

Oficio N° 13

Fecha	05-10-2018
Destinatario	**Superintendente del Medio Ambiente, señor Cristian Franz.**
Materia:	Solicitar, remita a la Comisión la información relacionada con el registro de las estaciones de monitoreo continuo de los últimos 12 meses de la zona correspondiente a las comuna de Concón, Quintero y Puchuncaví.
Respuesta:	Recibida el 5 de noviembre de 2018 mediante el cual informó el registro de monitoreo que incluye la evaluación de normas primarias de MP10, MP 2,5, SO2 y Pb, y la norma secundaria de SO2, correspondiente a los años 2015, 2016 y 2017.

Oficio N° 16

Fecha	08-10-2018
Destinatario	**Intendente Regional de Valparaíso, señor Jorge Martínez.**
Materia:	Solicitar, contemple un espacio de participación ciudadana en la toma de decisiones que afecten a la zona de Quintero, Puchuncaví, en todas y cada una de las materias que les involucre, especialmente en lo relacionado con el Plan de Descontaminación.
Respuesta:	Recibida el 26 de octubre de 2018 indicó que la consulta sobre espacio de participación ciudadana en la toma de decisiones que afectan a Quintero y Puchuncaví, fue remitida a la Seremi de Medio Ambiente de la región de Valparaíso, quien contestó que el proceso de participación Ciudadana para estas comunas comenzaría el 5 de noviembre y hasta el 14 de diciembre.

Oficio N° 21

Fecha	09-10-2018
Destinatario	**Subsecretario para Fuerzas Armadas, señor Juan Galli.**
Materia:	Con el propósito de hacerle presente que en futuras aprobaciones de Resolución de Calificación Ambiental se tenga

en consideración los efectos que eventualmente podría provocar el proyecto sometido a Estudio de Impacto Ambiental tanto en la contaminación de las ciudades como en la salud de las personas.

Oficio N° 22

Fecha 09-10-2018
Destinatario **Gobernador Marítimo de Valparaíso, señor Juan Gajardo.**
Materia: Hacer presente la sugerencia de la Comisión respecto a que en futuras aprobaciones de Resolución de Calificación Ambiental se tenga en consideración los efectos que eventualmente podría provocar el proyecto sometido a Estudio de Impacto Ambiental tanto en la contaminación de las ciudades como en la salud de las personas.

Oficio N° 23

Fecha 09-10-2018
Destinatario **Presidente Comisión Regional de Uso de Borde Costero de Valparaíso, señor Jorge Martínez.**
Materia: Con el propósito de solicitarle remita copias a esta Comisión de las actas en donde consta la aprobación de la concesión marítima que permite a la empresa Oxiquim S.A. la construcción y operación de un muelle multipropósito, en la bahía de Quintero.
Respuesta: Recibida el 26 de octubre de 2018 mediante el cual remitió antecedentes de la votación de la Comisión sin detalle.

Oficio N° 34

Fecha 13-11-2018
Destinatario Presidente Banco Mundial **señor Jim Yong Kim**
Materia: Solicitarle, en el más breve plazo, informe si el señor Marcelo Mena Carrasco, Gerente de Innovación de esa Institución, tendría alguna restricción para responder un cuestionarios sobre hechos ocurridos durante el ejercicio de su cargo como Ministro de Estado y Subsecretario en el Gobierno de la ex Presidenta señora Michelle Bachelet relacionados con la crisis ambiental que afectó a las comunas de Quintero, Puchuncaví y Concón.
Respuesta: Recibida el 14 de noviembre vía correo electrónico del representante del Banco Mundial en Chile, indica que realizará todas las gestiones pertinentes relacionadas con la declaración del señor Mena.

Oficio N° 37

Fecha 13-11-2018
Destinatario **Superintendente de Medio Ambiente(S), señor Rubén Verdugo.**
Materia: Con el propósito de solicitarle un informe del número histórico de Resolución de Calificación Ambiental que deben fiscalizar, la cantidad de fiscalizadores con los que históricamente ha contado para realizar sus funciones de fiscalización, separados por regiones, desde enero de 2010 hasta la fecha.

Respuesta: Recibida el 10 de diciembre de 2018 mediante el cual informó sobre el número histórico de Resolución de Calificación Ambiental, en estado de “aprobado”, o también aquellas calificadas favorablemente, y que el servicio maneja desde el 5 de noviembre de 2018 y la cantidad de fiscalizadores con los que cuenta la Superintendencia para realizar sus funciones separados por regiones.

Oficio N° 41

Fecha 19-11-2018

Destinatario **Seremi de Medio Ambiente**, **señora María Victoria Gazmuri.**

Materia: Con el propósito de solicitarle que remita a esta Instancia los antecedentes que obren en su poder, especialmente los oficios emitidos desde esa Seremía y los recibidos en relación con el trabajo multisectorial producto del diálogo entre actores del sector público, ciudadano y empresarial.

Respuesta: Recibida el 10 de diciembre de 2018 y remitió antecedentes sobre los oficios emitidos desde la Seremía del Medio Ambiente y los recibidos en relación con el trabajo multisectorial producto del dialogo entre actores del sector público, ciudadano y empresarial, en relación al Programa para la Recuperación Ambiental y Social para las comunas de Quintero y Puchuncaví.

Oficio N° 52

Fecha 20-12-2018

Destinatario **Superintendente de Medio Ambiente(S), señor Rubén Verdugo.**

Materia: Con el propósito de solicitarle informe sobre la metodología y obtención de datos con el equipo Thermo Scientific Miran Sapphire XL portable ambient analyzer. En particular, para que señale el significado y fuente del HQI expuesto en su informe de 23 de noviembre de 2018 (Ord. 2940 2018) y explique por qué descarta los datos en base a ese índice.

Respuesta: Recibida el 20 de enero de 2019, informó que de las mediciones realizadas con el monitor de gases Miran XL- Thermo Scientific entre el 22 de agosto y 25 de septiembre de 2018, se concluye que este equipo de medición no posee un nivel de certeza “HQI” aceptable para establecer conclusiones en relación a las mediciones realizadas. Adjuntó en formato CD, manual de instrucciones ThermoMatch, software que permite la extracción de los datos medidos y analizar su grado de certeza (HQI).

Oficio N° 55

Fecha 08-01-2019

Destinatario **Gobernador Marítimo de Valparaíso, señor Juan Gajardo.**

Materia: Informe la fecha en que la motonave Cabo Victoria descargó combustible en la bahía de Quintero; cuánto tiempo permaneció en dicha bahía, todas las operaciones que realizó desde la fecha de ingreso hasta la de salida del puerto, especialmente la operación de despiche y si estas operaciones se realizaron con supervisión de esa Gobernación controlando que se llevaran a cabo dentro de un circuito cerrado.

Respuesta: Recibida el 21 de enero de 2019.

OFICIOS CUYAS RESPUESTAS EXCEDIERON DE 30 DÍAS.

Oficio N° 02

Fecha	11-09-2018
Destinatario	**Ministro de Salud, señor Emilio Santelices.**
Materia:	informe los casos de nacimientos con mal formación o anormalidades atribuibles a la contaminación con metales pesados, sus patologías de ingreso, muertes prematuras y causas de estas muertes, en los últimos 15 años, detallado por cada Servicio de Salud a lo largo de Chile. Asimismo, los criterios utilizados para tomar los exámenes toxicológicos durante la emergencia ambiental en la zona contaminada, y el tipo de examen que se aplica, su alcance y cobertura. Además, remita registro de personas oriundas de Quintero y Puchuncaví que son atendidas en hospitales de otras comunas aledañas.
Respuesta:	Recibida el 29 de octubre de 2018.

Oficio N° 03

Fecha	11-09-2018
Destinatario	**Ministro de Salud, señor Emilio Santelices.**
Materia:	Solicita que la medición de metales pesados en las comunas de Quintero y Puchuncaví, que tenía considerado efectuar el año 2019, sea realizada durante este mes debido a la emergencia que afecta a la zona indicada.
Respuesta:	Recibida el 29 de octubre de 2018, informó que las mediciones de metales pesados y otras emisiones como la calificación de la misma como adversas en las comunas de Quintero y Puchuncaví es competencia del Ministerio del Medio Ambiente.

Oficio N° 04

Fecha	11-09-2018
Destinatario	**Director Nacional de ONEMI, señor Ricardo Toro.**
Materia:	Que indique si existe protocolo de emergencia ante las crisis ambientales por contaminación, como la que afectó a Quintero y Puchuncaví recientemente.
Respuesta:	Recibida el 29 de octubre de 2018, adjuntó informes técnicos de incidente o emergencia, asociados a este evento que se encuentra en desarrollo.

Oficio N° 05

Fecha	11-09-2018
Destinatario	**Intendente Regional de Valparaíso, señor Jorge Martínez.**
Materia:	Que indique si existe un protocolo de emergencia ante las situaciones de crisis ambientales por contaminación, como la que afectó a Quintero y Puchuncaví recientemente.
Respuesta:	Recibida el 26 de octubre de 2018 en el cual informó que el protocolo de emergencia ante situaciones de crisis lo maneja la Onemi, adjuntando la respuesta de esta institución.

Oficio N° 07

Fecha	11-09-2018
Destinatario	**Intendente Regional de Valparaíso, señor Jorge Martínez.**

Materia: remita un informe que contenga el listado y causas de las personas detenidas, con motivo de la marcha efectuada el día sábado 8 de septiembre, en la comuna de Quintero, especialmente la detención de doña Nicole Varas.

Respuesta: Recibida el 26 de octubre de 2018 respondió que en virtud del artículo 4 letra c de la ley 19.175, Ley Orgánica Constitucional, sobre Gobierno y Administración Regional, corresponde al gobernador de Valparaíso autorizar reuniones en plaza, calles y demás lugares de uso público.

Oficio N° 08

Fecha 11-09-2018

Destinatario **Ministro del Interior señor Andrés Chadwick.**

Materia: Que informe las medidas realizadas por esta institución, desde el 21 de agosto hasta la fecha, con motivo de lo ocurrido en Quintero y Puchuncaví.

Respuesta: Recibida el 26 de octubre informó las medidas adoptadas por el Ministerio en relación al problema ambiental que afecta a Quintero y Puchuncaví desde el 21 de agosto hasta el 25 de octubre, fecha del informe.

Oficio N° 17

Fecha 05-10-2018

Destinatario **Gobernadora de Valparaíso, señora María de Los Ángeles de la Paz Riveros.**

Materia: Solicitar, contemple un espacio de participación ciudadana en la toma de decisiones que afecten a la zona de Quintero y Puchuncaví, en todas y cada una de las materias que les involucre, especialmente en lo relacionado con el Plan de Descontaminación.

Respuesta: Recibida el 17 de diciembre de 2018 informó que se encuentra en desarrollo el proceso de elaboración del plan de prevención y de descontaminación atmosférica, para las comunas antes dichas el que contempla un espacio de participación ciudadana o periodo de consulta ciudadana vigente hasta el 14 de diciembre. Asimismo indicó que el 31 de diciembre es la fecha máxima para el ingreso del plan de prevención y descontaminación a la Contraloría General de la República.

Oficio N° 24

Fecha 09-10-2018

Destinatario **Seremi de Medio Ambiente**, **señora María Victoria Gazmuri.**

Materia: Con el propósito de solicitarle remita a esta Comisión el contenido del CD adjunto al MEMO N° 262/2016 del 12 octubre de 2016 del SEREMI Medio Ambiente dirigido al señor Germán Oyola, Jefe de la División de Calidad del Aire del Ministerio Ambiente de la época, relativo a la propuesta de proyecto definitivo del Plan de Descontaminación Atmosférica para las comunas de Concón, Quintero y Puchuncaví.

Respuesta: Recibida el 21 de diciembre de 2018, en donde adjuntó CD solicitado y aclaró que este CD es un documento preliminar de una propuesta del proyecto definitivo del Plan de Descontaminación Atmosférica para las comunas de Concón, Quintero y Puchuncaví, el cual no es un documento oficial y que fue remitido a Santiago, al Ministerio del Medio Ambiente al jefe

de División de Calidad del Aire para fines de revisión, modificación y apoyo para el Plan definitivo.

Oficio N° 26

Fecha 09-10-2018
Destinatario **Ministro de Salud, señor Emilio Santelices.**
Materia: Solicitarle que remita los resultados del informe realizado por la Organización Mundial de la Salud con el detalle de las acciones y recomendaciones que esta institución dirigió a esa Cartera, a propósito de los episodios de contaminación en Quintero y Puchuncaví.
Respuesta: Recibida el día 17 de diciembre de 2018 remitió los documentos que contienen los resultados del informe de cooperación técnica OPS/OMS, realizado a propósito de los episodios de contaminación Quintero y Puchuncaví del pasado agosto.

Oficio N° 27

Fecha 09-10-2018
Destinatario **Ministro de Salud, señor Emilio Santelices.**
Materia: Consultar razones por las cuales no ha considerado el ofrecimiento que realizó la Unicef relativo a un plan de apoyo psicológico en favor de los niños pertenecientes a la zona afectada por la contaminación en Quintero y Puchuncaví.
Respuesta: Recibida el 20 de diciembre de 2018 detalló las acciones que la Unicef ha realizado en la zona afectada y que consiste específicamente en repartir material impreso, guías para familias y cartillas para niños, asimismo adjuntó el reporte de acciones y líneas de trabajo en el ámbito de salud mental y apoyo psicosocial realizado en el marco de la emergencia Quintero, Puchuncaví, actualizado al 11 de noviembre.

Oficio N° 28

Fecha 29-10-2018
Destinatario **Superintendente de Electricidad y Combustible, señor Luis Ávila.**
Materia: Informe las fiscalizaciones y sus resultados sobre el cumplimiento de la normativa legal y técnica por parte de la empresas que conforman el complejo Industrial Ventanas y que participan en la generación, producción, almacenamiento, transporte y distribución de combustibles líquidos, gas y electricidad.
Respuesta: Recibida el 10 de diciembre de 2018. Adjuntó documentos con la información requerida.

Oficio N° 29

Fecha 29-10-2018
Destinatario **Ministro de Salud, señor Emilio Santelices.**
Materia: Solicitar que informe todas y cada una de las medidas adoptadas por esa Cartera en la esfera de sus competencia, a propósito de los episodios de contaminación en Quintero y Puchuncaví, desde el 21 de agosto a la fecha.
Respuesta: Recibida el 21 de enero de 2019, informa sobre cuales han sido las acciones en: atención en salud, de promoción de salud, de

prevención y fiscalización sanitaria, de salud pública, y la implementación de la alerta sanitaria de fecha 24 de septiembre de 2018.

Oficio N° 30

Fecha	29-10-2018
Destinatario	**Ministra del Medio Ambiente, señora Carolina Schmidt.**
Materia:	Remita las memorias de cálculo mediante las cuales se construyeron las diversas tablas del plan de Prevención y Descontaminación Atmosférica de Concón, Quintero y Puchuncaví, representado por la Contraloría General de la República.
Respuesta:	Recibida el 7 de enero de 2019 respondió que es imposible remitir las memorias porque estas estimaciones se realizaron con un modelo elaborado mediante software Anlytica, que no corresponde a una planilla de cálculo simple, sin embargo detalló referencias bibliográficas mediante las que se puede hacer la trazabilidad de la evaluación económica del plan.

Oficio N° 32

Fecha	29-10-2018
Destinatario	**Superintendente del Medio Ambiente, señor Cristian Franz**.
Materia:	Solicitar remitir el listado de las industrias y empresas que funcionan en el cordón industrial correspondiente a las comunas de Concón, Quintero y Puchuncaví., con el detalle de sus resoluciones de calificación ambiental vigentes.
Respuesta:	Recibida el 10 de diciembre de 2018 con el detalle pedido.

Oficio N° 38

Fecha	13-11-2018
Destinatario	**Alcalde de Quintero**, **señor Mauricio Carrasco.**
Materia:	Se adjunta cuestionario con preguntas.
Respuesta:	Recibida el 21 de enero de 2019.

Oficio N° 39

Fecha	13-11-2018
Destinatario	**Alcaldesa de Puchuncaví, señora Eliana Olmos.**
Materia:	Se adjunta cuestionario con preguntas.
Respuesta:	Recibida el 7 de enero de 2019.

Oficio N° 40

Fecha	13-11-2018
Destinatario	**Alcalde de Concón, señor Oscar Sumonte.**
Materia:	Se adjunta cuestionario con preguntas.
Respuesta:	Recibida el 21 de enero de 2019.

OFICIOS SIN RESPUESTAS

Oficio N° 12

Fecha	05-10-2018
Destinatario	**Ministro de Salud, señor Emilio Santelices.**
Materia:	Solicitar informe los criterios para realizar examen de sangre que advierte la presencia de metales pesados e indique razones por la que no se han realizado en las comunas de Quintero y Puchuncaví, con ocasión de los episodios de crisis ambiental vividos el año 2018.

Oficio N° 14

Fecha	05-10-2018
Destinatario	**Directora de Sernapesca, señora Alicia Gallardo.**
Materia:	Solicitar, realice un estudio y la fiscalización en caletas y Áreas de Manejo de la zona Litoral Quinta Norte.

Oficio N° 18

Fecha	05-10-2018
Destinatario	**Alcaldesa de Puchuncaví**, **señora Eliana Olmos.**
Materia:	Solicitar, contemple un espacio de participación ciudadana en la toma de decisiones que afecten a la zona de Quintero y Puchuncaví, en todas y cada una de las materias que les involucre, especialmente en lo relacionado con el Plan de Descontaminación.

Oficio N° 19

Fecha	05-10-2018
Destinatario	**Alcalde de Quintero**, **señor Mauricio Carrasco.**
Materia:	Solicitar, contemple un espacio de participación ciudadana en la toma de decisiones que afecten a la zona de Quintero y Puchuncaví, en todas y cada una de las materias que les involucre, especialmente en lo relacionado con el Plan de Descontaminación.

Oficio N° 33

Fecha	29-10-2018
Destinatario	**Ministro de Obras Públicas, señor Juan Fontaine.**
Materia:	Remita listado de las industrias y empresas que funcionan en el cordón industrial correspondiente a las comunas de Concón, Quintero y Puchuncaví., con el detalle de sus resoluciones de calificación ambiental vigentes.

Oficio N° 35

Fecha	13-11-2018
Destinatario	**Contralor General de la República, señor Jorge Bermúdez.**
Materia:	Informe si el Plan de Prevención de Contaminación Atmosférica para la localidad de Huasco fue objeto de observación relativa al aumento de inventario en relación a su anteproyecto (reiterado).

Oficio N° 36

Fecha	13-11-2018
Destinatario	**Ministro de Hacienda, señor Felipe Larraín.**

Materia: Informe los presupuestos históricos asignado al Ministerio de Medio Ambiente, a la Superintendencia de Medio Ambiente y al Servicio de Evaluación Ambiental, desde enero de 2010, fecha en que fueron creados por la ley N° 20.417 hasta la actualidad.

Oficio N° 42
Fecha 26-11-2018
Destinatario **Señor Marcelo Mena Carrasco.**
Materia: Se hace llegar un cuestionario formulado por la Comisión.
Respuesta: Sin respuesta y reiterado nuevamente sin respuesta. .

Oficio N° 43
Fecha 13-12-2018
Destinatario **Ministra del Medio Ambiente, señora Carolina Schmidt.**
Materia: Con el propósito a que remita los informes enviados a propósito de los recursos de protección acumulados en causa Rol 7266 2018 en la Corte de Apelaciones de Valparaíso.

Oficio N° 42
Fecha 13-12-2018
Destinatario **Señor Germán Oyola.**
Materia: Con el propósito de solicitarle que remita a esta Instancia, los criterios de la metodología bajo los cuales se determinó los niveles de emisión consignados en el inventario de emisiones, respecto de las fuentes puntuales (Codelco, Enap y AES Gener).

Oficio N° 45
Fecha 17-12-2018
Destinatario **Ministra del Medio Ambiente, señora Carolina Schmidt.**
Materia: Con el objeto de que informe sobre cuales han sido las medidas adoptadas en las comunas de Huasco y Coronel desde 1990 en adelante.

Oficio N° 46
Fecha 17-12-2018
Destinatario **Ministro de Salud, señor Emilio Santelices.**
Materia: Con el objeto de solicitar se realicen exámenes toxicológicos a los habitantes de las Comuna de Coronel y Huasco.

Oficio N° 47
Fecha 18-12-2018
Destinatario **Ministra del Medio Ambiente, señora Carolina Schmidt.**
Materia: Con el propósito de solicitarle, disponga que en la página web del Ministerio que encabeza un banner con información permanente acerca de la calidad del aire y las condiciones de ventilación en las comunas que forman parte de la mal denominada zonas de sacrificio, tales como Huasco, Tocopilla, Mejillones, Coronel, entre otras, tal como se realiza actualmente para las comunas de Quintero Puchuncaví.

Oficio N° 48
Fecha 18-12-2018
Destinatario **Director General Policía de Investigaciones de Chile, señor Héctor Espinosa.**
Materia: Con el propósito de que precise los fundamentos del allanamiento efectuado en ENAP Biobío por personal de su institución e indique de qué forma estaría relacionado con la crisis ambiental vivida en Quintero Puchuncaví en agosto y septiembre pasado.

Oficio N° 49
Fecha 18-12-2018
Destinatario **Director del Servicio de Evaluación Ambiental, señor Hernán Brücher.**
Materia: Informe la cantidad de proyectos industriales ubicados en la bahía de Concón, Quintero y Puchuncaví, que han sido modificados por vía de pertinencia, con mención expresa del solicitante, fecha de solicitud y de la aprobación de las mismas.

Oficio N° 50
Fecha 18-12-2018
Destinatario **Director del Servicio de Evaluación Ambiental, señor Hernán Brücher.**
Materia: Informe las pertinencias vigentes respecto de proyectos industriales emplazados en Coronel, Mejillones, Huasco, Tocopilla y en la bahía de Quintero.

Oficio N° 51
Fecha 20-12-2018
Destinatario **Ministra del Medio Ambiente, señora Carolina Schmidt**.
Materia: Informe las medidas adoptadas en las comunas de Huasco y Coronel desde 1990 en adelante.

Oficio N° 53
Fecha 09-01-2019
Destinatario **Subsecretario para Fuerzas Armadas, señor Juan Galli.**
Materia: Con el propósito que informe acerca de los siguientes antecedentes: a) Si tienen conocimiento del informe realizado el año 2009 por la Armada de Chile en el cual se advirtió que el tráfico marítimo existente en la bahía de Quintero estaba saturado y no era posible incrementarlo; b) Si la Armada de Chile actualizó este informe en consideración al impacto que tendrá el muelle de Oxiquim, recientemente aprobado en relación al tráfico marítimo.

Oficio N° 54
Fecha 09-01-2019
Destinatario **Gobernador Marítimo de Valparaíso, señor Juan Gajardo.**
Materia: Solicita información acerca de los siguientes antecedentes: a) Medidas adoptadas frente a los varamientos de carbón producidos en la playa de Ventanas, especialmente el acontecido el 6 de enero pasado, tomando en consideración el uso recreativo que se le da a esta playa contaminada; b) Si se

ha instruido investigación sumaria administrativa al respecto para buscar eventuales responsabilidades. Asimismo se le solicita, adoptar todas las medidas pertinentes dentro de sus facultades legales para evitar el ingreso de personas a la playa contaminada, mientras el carbón no sea retirado.

V.- CONSIDERACIONES, CONCLUSIONES Y PROPUESTAS.

Es preciso consignar que producto del debate habido en el seno de esta Comisión en la sesiones celebradas los días 21 y 22 de enero de 2019, prorrogada legal y reglamentariamente, se presentó por parte de los integrantes para su estudio, debate y posterior votación, un documento con conclusiones, y proposiciones o recomendaciones; la mayoría ya consensuadas, no obstante existir diferencias en algunos puntos, por lo que se acordó por unanimidad votar separadamente algunas de las conclusiones, y las recomendaciones propuestas y que se detallan más adelante.

Se deja constancia que ante esta Secretaría se presentó un documento que contenía propuestas y recomendaciones del diputado señor Amaro Labra, que fueron recogidas en el texto final, así como una constancia de la diputada señora Carolina Marzán.

A continuación se transcribe el texto íntegro de cada una las conclusiones y recomendaciones que fueron estudiadas y votadas por los integrantes de la Comisión, junto al debate y la votación respectiva, para finalmente consignar las conclusiones y recomendaciones aprobadas.

DISCUSIÓN Y VOTACIÓN DE LAS CONCLUSIONES Y PROPOSICIONES.

El diputado **Ibáñez** (Presidente) explica que se ha elaborado y en parte consensuado por los diputados y diputadas de la Comisión un borrador que se tiene como documento base, con las conclusiones y proposiciones sobre la investigación.

Al respecto, se acuerda dar lectura y votar separadamente las conclusiones y proposiciones o recomendaciones planteadas, para tratar de alcanzar acuerdo en aquellas en que todavía hay discrepancias y presentar un informe de consenso.

A continuación se consigna el tratamiento dado por la Comisión a cada una de las conclusiones y recomendaciones:

CONCLUSIÓN N° 1.

Declara que los problemas ambientales que sufren las comunas de Quintero y Puchuncaví se han mantenido sin solución por las diferentes autoridades administrativas de turno, evidenciándose diferentes tipos y niveles de responsabilidades.

El diputado **Pardo** solicita agregar el término “y políticas” a continuación de la frase “diferentes autoridades”.

No presentándose objeciones a la conclusión N° 1 propuesta, se somete a votación, siendo aprobada en los mismos términos con la corrección propuesta, en

forma unánime, por 10 votos a favor, de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 2.
Respecto a la responsabilidad sobre el plan de descontaminación Concón, Quintero y Puchuncaví.

El diputado **Verdessi** manifestó que de las declaraciones vertidas por el ex Ministro de Medio Ambiente en la Comisión queda claro que al señor Pablo Badenier no le cabe responsabilidad políticas en relación al fallido plan de descontaminación para la zona, Lo anterior por cuanto de sus dichos se puede advertir una responsabilidad del Ministerio de Medio Ambiente, como órgano, sin que recaiga en él específicamente, toda vez que en su declaración no hay contradicción alguna que haga dudar de su convencimiento de que no se cometió un error en su elaboración sino que hubo un cambio estructural.

La conclusión N° 2 propuesta, se somete a votación, siendo aprobada en los mismos términos por mayoría de votos (9 votos a favor, 1 voto en contra) Por la afirmativa votaron los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas y Saffirio, en contra lo hizo el diputado Verdessi.

CONCLUSIÓN N° 3.
Referido a que el plan de descontaminación para las zonas de Quintero y Puchuncaví, fue representado por no ajustarse a derecho. La elaboración del plan de descontaminación y por tanto, la decisión confeccionar un inventario de emisiones superior al que correspondía fue realizada durante la gestión del ex Ministro de Medio Ambiente Sr. Pablo Badenier. Si bien, tanto él y aunque éstos defienden la metodología, la Comisión comparte el criterio de la Contraloría General de la República en cuanto que no cumplía con su objetivo legal.

La conclusión N° 3 propuesta, se somete a votación, siendo aprobada en los mismos términos por unanimidad, con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 4.
El hecho de no haber subsanado las observaciones que hizo la Contraloría General de la República al plan durante la gestión del ex Ministro de Medio ambiente Marcelo Mena, lo hacen responsable políticamente de este hecho, puesto que existiendo todas las posibilidades para subsanar los reparos y permitir contar con un plan de descontaminación vigente para la zona, optó por no hacer nada lo que implica una manifiesta falta a sus responsabilidades como Ministro de Estado.

La Comisión dejó constancia en este punto que resulta inaceptable que el señor Marcelo Mena no haya concurrido a declarar a la Comisión ni tampoco haya respondido las preguntas que se le hicieran llegar toda vez que pudo haber contribuido al trabajo de la Comisión.

El diputado **Saffirio** sugirió establecer la responsabilidad acorde a lo expresado en el artículo 52 letra b de la Constitución Política, esto es dejar sin

ejecución una norma. No obstante el diputado **Kast** hizo presente que en este caso no hay una norma que se haya dejado sin ejecutar.

Sometida a votación la conclusión N° 4 en los mismos términos propuestos, resulto aprobada por mayoría de votos (7 votos a favor, 2 en contra y 1 abstención). Votaron a favor los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Longton, Marzán, Pardo y Verdessi, en contra lo hicieron los diputados Labra y Saffirio, en tanto se abstuvo el diputado Rosas.

CONCLUSIÓN N° 5.

Señala que de lo informado por diversos invitados, se concluye que en el proceso de revisión de las observaciones al plan de descontaminación, no se involucró a la SEREMI de Medio Ambiente de Valparaíso.

La conclusión N° 5 propuesta, se somete a votación, siendo aprobada en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 6

.Precisa que las diferencias entre el inventario de emisiones que llevó a la representación del plan de descontaminación atmosférica con el inventario basado en emisiones reales, producía un beneficio a la empresas más contaminantes del parque industrial, como a AES Gener se le permitía holgura para emitir más toneladas de los tres contaminantes, a CODELCO más SO2 y a ENAP más NOx.

La conclusión N° 6 propuesta, se somete a votación, siendo aprobada en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

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CONCLUSIÓN N° 7

Indica que el ordenamiento jurídico no contempla faltas administrativas que pudieran implicar sanciones ante los hechos constatados. Lo que es más complejo cuando los plazos para abrir procesos administrativos han caducado.

El diputado **Pardo** propone establecer que el ordenamiento jurídico es insuficiente para perseguir faltas administrativas y agregar como oración final la siguiente “Sin perjuicio de existir una eventual infracción por parte del ex ministro Marcelo Mena Carrasco al artículo 52 N° 2, letra b), de la Constitución Política de la República, al no responder oportunamente las observaciones de la Contraloría General de la República formuladas al plan de descontaminación representado. Así se constata que nuestro ordenamiento jurídico es débil e insuficiente para sancionar faltas administrativas e infracciones legales por parte de las autoridades responsables del medioambiente”.

La conclusión N° 7 propuesta, con la sugerencia indicada, es aprobada por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 8

El párrafo primero se refiere a los beneficios que cuantificaba el propio plan rechazado.

Por el párrafo segundo se constata que la sola existencia del plan no resultaba suficiente para evitar los episodios de intoxicaciones, sin embargo la Comisión considera que su vigencia podría haber contribuido principalmente por los límites a las emisiones que contemplaba.

Por el párrafo tercero se valora el esfuerzo del gobierno actual en impulsar con urgencia el plan de descontaminación como parte de las medidas adoptadas para entregar una solución a los problemas de contaminación que afectan a la zona.

El párrafo cuarto prescribe que el plan de descontaminación es una herramienta insuficiente por sí solo para hacerse cargo de contaminación que afecta a la zona por más de 50 años. Esto porque en el objetivo del plan es dar cumplimiento a normas de calidad del aire, las que tienen estándares insuficientes que debería ajustarse a los niveles propuestos por la OMS.

El diputado **Verdessi** manifiesta su desacuerdo con el párrafo segundo pues considera que no se puede afirmar que la vigencia del plan podría haber evitado los episodios de intoxicaciones y por ende es una suposición que no está demostrada científicamente y adelanta su voto en contra.

El diputado **Pardo** argumenta que resulta obvio que es beneficioso para los problemas de contaminación contar con un plan de descontaminación pues disminuyen los niveles de contaminación.

El diputado Labra respecto del párrafo tercero considera que es inoficioso resaltar los esfuerzos de un gobierno por un plan que no está aprobado ni vigente.

El diputado **Longton** solicita agregar una oración final en el párrafo tercero que haga alusión a los plazos de participación ciudadana tanto del actual plan elaborado como del anterior objetado.

El diputado **Verdessi** señala que el párrafo cuarto es contradictorio con el primero porque indica que el plan es un instrumento insuficiente, no obstante el segundo indica que de haber estado vigente podría haber contribuido a la descontaminación principalmente por los límites a las emisiones que contemplaba.

Se acuerda votar por separados los párrafos segundo y tercero.

Los párrafo primero y cuarto propuestos son aprobados en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

El párrafo segundo propuesto es aprobado en los mismos términos por mayoría de votos (7 votos a favor y 3 en contra). Por la afirmativa votaron los diputados José Miguel Castro, Ibáñez, Kast, Longton, Pardo, Saffirio y Verdessi, en contra lo hicieron los diputados Labra, Marzán, Rosas.

El párrafo tercero propuesto es aprobado con la sugerencia del diputado Longton por mayoría de votos (7 votos a favor y 3 en contra). Por la afirmativa votaron los diputados José Miguel Castro, Ibáñez, Kast, Longton, Pardo, Saffirio y Verdessi, en contra lo hicieron los diputados Labra, Marzán, Rosas.

CONCLUSIÓN N° 9

Prescribe que la grave crisis ambiental y social vivida en la zona de Quintero y Puchuncaví es el reflejo de un fracaso sistemático del Estado en relación a las medidas que se han adoptado en los últimos cincuenta años como garante del derecho a vivir en un medio ambiente libre de contaminación, que por cierto, no es posible atribuir a un gobierno en particular.

La conclusión N° 9 propuesta, se somete a votación, siendo aprobada en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 10

Declara que la Comisión Investigadora creada el año 2011 puso en evidencia un conjunto de condiciones y elementos que llevaron a las comunas de Quintero, Puchuncaví y Concón a tener altos niveles de contaminación en aire, agua y suelo e hizo un conjunto de recomendaciones para que el Estado tomará medidas, sin embargo sólo algunas fueron tomadas en cuenta.

El diputado **Verdessi** sugiere entre las medidas que no fueron adoptadas agregar “el aseo de las escuelas que debía repetirse anualmente”.

La conclusión N° 10 propuesta, con la sugerencia indicada, se somete a votación, siendo aprobada en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 11

Se refiere a la responsabilidad que le cabe a la Cámara de Diputados por recomendaciones efectuadas por la comisión investigadora del año 2011 en el seguimiento de las recomendaciones que emanaron del trabajo de la Comisión investigadora.

La conclusión N° 11 propuesta, se somete a votación, siendo aprobada en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 12

Atribuye al estado una responsabilidad al no planificar y ejecutar políticas públicas que pudieran prevenir, frenar o resolver el creciente proceso contaminación, al cual se encuentra expuesta las comunidades y el medio ambiente de las zonas afectadas.

Se propone agregar después del punto final la oración “, identificando una falta de herramientas por parte del Ministerio del Medio Ambiente para liderar una evolución del Estado en este sentido”.

La conclusión N° 12 propuesta, con la sugerencia indicada, se somete a votación, siendo aprobada en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 13

Señala que el gobierno central y regional no contó con recursos, ni capacidad de gestionar una respuesta ante la crisis ambiental, pues no existe un plan de emergencia y de respuesta frente a catástrofes ambientales. Ello significó una actuar errático desde el gobierno, que no permitió actuar a tiempo y evitar el gran número de intoxicaciones y el daño ambiental.

El diputado **Saffirio** sugiere agregar a continuación de la palabra "recursos" la frase "humanos, jurídicos y tecnológicos".

El diputado **Pardo** propone reemplazar en la oración "La ausencia de estos planes, trajo como consecuencia una actuar errático desde el gobierno" el término "errático" por "insuficiente",

El diputado **Labra** sugiere agregar al término "errático" la expresión "y insuficiente".

La conclusión N° 13 propuesta, con las sugerencias indicadas por los diputados Saffirio y Labra, se somete a votación, siendo aprobada por mayoría de votos (6 votos a favor y 4 votos en contra). Votaron por la afirmativa los diputados Ibáñez, Labra, Marzán, Rosas, Saffirio y Verdessi, en contra lo hicieron los diputados José Miguel Castro, Kast, Longton y Pardo.

CONCLUSIÓN N° 14

Se refiere a la insuficiente respuesta del Gobierno a la emergencia, sin perjuicio de que las responsabilidades políticas particulares, que corresponderían tanto al gobierno regional como al gobierno central, responden principalmente a una debilidad institucional del Estado. Lo anterior permite entender una gestión de la emergencia "a ciegas", toda vez que no se contaba, ni con los instrumentos de gestión ambiental adecuados, ni con equipos de medición y fiscalización suficientes.

La conclusión N° 14 propuesta, con la sugerencia indicada, se somete a votación, siendo aprobada en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIÓN N° 15

La Comisión no comparte la decisión de suspender las clases por la emergencia, sino más bien, considera que se debieron tomar medidas para disminuir o suspender la actividad industrial que podía originar la contaminación.

La conclusión N° 15 propuesta, se somete a votación, siendo aprobada por mayoría de votos (6 votos a favor y 3 votos en contra). Votaron por la afirmativa los diputados Ibáñez, Labra, Marzán, Rosas, Saffirio y Verdessi, en contra lo hicieron los diputados José Miguel Castro, Longton y Pardo.

CONCLUSIÓN N° 16

Relativa a la no respuesta de un oficio a la Superintendencia de Medio Ambiente para que aclare lo expuesto en su informe del 23 de noviembre de 2018 sobre los datos de medición del equipo MIRAN XL.

Esta conclusión se elimina por unanimidad en atención a que dicho oficio precisamente fue respondido el día de hoy. Participaron en la votación los diputados José Miguel Castro, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, Rosas, Saffirio y Verdessi.

CONCLUSIONES N°s 17 a 22 (que han pasado a ser N°s 16 a 21).

Se acuerda votarlas en conjunto

Las conclusiones propuestas, se somete a votación, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

CONCLUSIÓN N° 23 (que ha pasado a ser 22)

Se refiere que el Plan Regulador Metropolitano del Gran Valparaíso y sus modificaciones destinaron a Quintero-Puchuncaví como una "zona de sacrificio", toda vez que permitió que se instalará -y que sucesivamente se expandiera- un sobredimensionado parque industrial. Asimismo menciona la aprobación por la Comisión del Borde Costero de la Región de Valparaíso, de una modificación de la concesión marítima de la empresa Oxiquim S.A. en la bahía de Quintero, para construir y operar un muelle mecanizado multipropósito

El diputado **Verdessi** presenta una conclusión para agregar un párrafo segundo del siguiente tenor: "Posteriormente se realizó una nueva reunión de la Comisión de Uso del Borde Costero para ratificar el acta, la que fue rechazada por los alcaldes y por los consejeros, sin embargo resultó aprobada con los votos de los funcionarios de gobierno que forman parte de esa Comisión, lo que es responsabilidad del Intendente señor Jorge Martínez Durán.

La conclusión propuesta, se somete a votación en conjunto con la presentada por el diputado Verdessi, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

CONCLUSIÓN N° 24 (que ha pasado a ser 23)

Indica que la emergencia evidencia que no ha existido por parte del Estado la voluntad de dictar las normas necesarias de aire, agua y suelo o ni de dotado a los órganos correspondientes de mayores atribuciones para responder ante la crisis ambiental. Asimismo señala que la Comisión Investigadora del año 2011 recomendó normas más exigentes, sin embargo salvo excepciones no fueron atendidas

El diputado **Pardo** presenta una propuesta para precisar algunas de las medidas adoptadas por el gobierno ante esta crisis, como el nuevo plan de descontaminación, una oficina de la Superintendencia del Medioambiente, con asiento en Quintero, con dedicación exclusiva a la fiscalización del parque industrial; compromiso establecido en el nuevo PDA para el rediseño y modernización de la red de monitoreo que quedará bajo tuición del Estado.

La conclusión propuesta, se somete a votación en conjunto con la presentada por el diputado Pardo, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

CONCLUSIÓN N° 25 (que ha pasado a ser 24)

Prescribe que uno de los elementos por los que se desata la emergencia en la zona, es por la falta de una normativa eficiente y eficaz que impida la emanación de contaminantes, y que establezca procedimientos y sanciones estrictas en caso de incumplimiento.

El diputado **Pardo** presenta un párrafo final a la conclusión propuesta del siguiente tenor: “En este sentido, resulta valorable, el ingreso a la Contraloría General de la república de la Norma Primaria de Calidad de Aire para Dióxido de Azufre, de alcance nacional, que tiene como objetivo proteger la salud de las personas de los efectos agudos y crónicos generados por la exposición a concentraciones en el aire de dióxido de azufre (SO2). Esta nueva norma incorpora de forma inédita el valor de una hora, en línea con lo que ocurre a nivel mundial debido a que los efectos en la salud de este contaminante se evidencian especialmente después de peaks de dióxido de azufre (SO2) de corta duración, muy frecuentes en zonas industriales con presencia de fundiciones de cobre y termoeléctricas a carbón. Cabe señalar que esta norma se ajustaría a estándares de norma europea mas no se ajustaría a los estándares propuestos por las organizaciones internacionales como la Organización Mundial de la Salud.”,

La conclusión propuesta, se somete a votación en conjunto con la presentada por el diputado Pardo, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

CONCLUSIONES N°s 26 a 33 (que han pasado a ser N°s 25 a 32).

Se acuerda votarlas en conjunto

Las conclusiones propuestas, se somete a votación, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

CONCLUSIÓN N° 34 (que ha pasado a ser 33)

Precisa que aunque ninguna de las fiscalizaciones y sumarios han podido determinar con certeza responsabilidad de alguna empresa del parque en los episodios de contaminación, todas cooperan de forma permanente en la contaminación, además de que gran parte de ellas no cumple la normativa ambiental vigente.

El diputado **Kast** presenta un párrafo final a la conclusión propuesta del siguiente tenor: “Se debe dejar constancia que en la actualidad hay una investigación en curso que se está llevando adelante por el Ministerio Público, que busca establecer si existió un nexo entre el trasvasije de más de 80 mil metros cúbicos de petróleo iraní el 3 de agosto del año 2018 desde el Monte Toledo, un barco procedente de Irán con bandera portuguesa, hacia el Cabo Victoria, propiedad de Enap y que, luego de trasvasijar su contenido, navegó hacia el norte, precisamente, hacia el eje industrial de Quintero y Puchuncaví, lo cual no ha permitido a esta comisión poder contar con todos los antecedentes a la vista”.

Se acuerda votar por separados los párrafos.

El párrafo primero propuesto es aprobado en los mismos términos por unanimidad con los votos de los diputados (as) señores (as) Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

El párrafo segundo propuesto es rechazado por 3 votos a favor y 4 en contra). Por la afirmativa votaron los diputados Kast, Longton y Pardo, en contra lo hicieron los diputados Ibáñez, Labra, Marzán y Verdessi.

CONCLUSIONES N°s 35 a 43 (que han pasado a ser N°s 34 a 42).

Se acuerda votarlas en conjunto

Las conclusiones propuestas, se somete a votación, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

CONCLUSIÓN N° 44

La Diputada Marzán presenta una consideración del siguiente tenor:

“Finalmente esta Comisión Investigadora hace presente su descontento ante la escasa colaboración de algunos Órganos del Estado, de la Administración del Estado, autoridades y exautoridades de gobierno o municipales, por la poca celeridad en responder oficios de importancia para el cumplimiento del objetivo de la Comisión. Resultaba de especial relevancia el compromiso de los órganos públicos para contribuir en el desarrollo de la labor de la Comisión Investigadora en orden a esclarecer puntos controvertidos. Sin ir más lejos, aún hay oficios sin responder y otros que fueron respondidos fuera de plazo, lo que demuestra la exigua disposición de algunos a colaborar.

En específico, referente a lo precitado, los órganos y oficios en dicho estado se encuentran:

- Oficios cuyas respuestas excedieron de 30 días dirigidos: la Ministra del Medio Ambiente, señora Carolina Schmidt; al Ministro del Interior señor Andrés Chadwick; al Director Nacional de ONEMI, señor Ricardo Toro; al Intendente Regional de Valparaíso, señor Jorge Martínez; a la Gobernadora de Valparaíso, señora María de Los Ángeles de la Paz Riveros; a la Seremi de Medio Ambiente, señora María Victoria Gazmuri; al Superintendente de Electricidad y Combustible, señor Luis Ávila; al Superintendente del Medio Ambiente; al Alcalde de Quintero, señor Mauricio Carrasco; a la Alcaldesa de Puchuncaví, señora Eliana Olmos, y al Alcalde de Concón, señor Oscar Sumonte.

- Oficios no respondidos por: el Ministro de Salud, señor Emilio Santelices; el Ministro de Obras Públicas, señor Juan Fontaine; la Ministra del Medio Ambiente, señora Carolina Schmidt; el Ministro de Hacienda, señor Felipe Larraín; el Contralor General de la República, señor Jorge Bermúdez; el Subsecretario para Fuerzas Armadas, señor Juan Galli; la Directora de Sernapesca, señora Alicia Gallardo; el Director del Servicio de Evaluación Ambiental, señor Hernán Brücher; el Director General Policía de Investigaciones de Chile, señor Héctor Espinosa; el Gobernador Marítimo de Valparaíso, señor Juan Gajardo; la Alcaldesa de Puchuncaví, señora Eliana Olmos; el Alcalde de Quintero, señor Mauricio Carrasco; el ex Ministro y ex

Subsecretario de Medio Ambiente, señor Marcelo Mena Carrasco, y el ex jefe de la División de la calidad del Aire del Ministerio de Medio Ambiente, señor Germán Oyola.

Entrando en el análisis de las recomendaciones propuestas en el documento que sirve de base a su discusión, la Comisión adopta los siguientes acuerdos:

RECOMENDACIONES N°s 1 a la 14.

Se acuerda votarlas en conjunto

Las recomendaciones propuestas, se somete a votación conjunta, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

RECOMENDACIÓN N° 14.
Señala que si bien las emisiones de las empresas del parque industrial se deben medir y controlar de forma individual, es fundamental establecer una norma de medición que considere la sumatoria de las emisiones de todas las empresas del parque industrial.

La Comisión acuerda agregar como frase final la siguiente: “Se propone como política de Estado la introducción de industria descontaminante asociada a los complejos industriales, incorporando la experiencia internacional.”.

La recomendación propuesta, se somete a votación conjunta, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

RECOMENDACIONES N°s 15 y 16.

Se acuerda votarlas en conjunto

Las recomendaciones propuestas, se somete a votación conjunta, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

RECOMENDACIÓN N° 17.
Propone aplicar los cambios regulatorios necesarios para que los proyectos que no cuentan con Resolución de Calificación Ambiental (RCA) y cuyas características de impactos ambientales así lo ameriten se sometan al SEIA, además se debe fortalecer la institucionalidad ambiental, especialmente la labor fiscalizadora de la Superintendencia de Medio Ambiente, en particular las empresas más antiguas se encuentran al margen de la ley.

La Comisión acuerda reemplazar al final la expresión “al margen de la ley” por la palabra “desreguladas”.

La recomendación N° 17 propuesta, se somete a votación conjunta, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

RECOMENDACIONES N°s 18 a 20

Se acuerda votarlas en conjunto

Las recomendaciones propuestas, se somete a votación conjunta, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

RECOMENDACIÓN N° 21.

Sugiere al Estado promover las mejores prácticas sobre el acceso a la información, participación pública y acceso a la justicia en asuntos ambientales conforme a los tratados internacionales sobre derechos humanos, en línea con lo establecido con el Acuerdo Regional sobre el Acceso a la Información, la Participación Pública, y el Acceso a la Justicia en Asuntos Ambientales en América Latina y el Caribe, conocido como el Acuerdo de Escazú, esto con el objeto de resguardar el derecho de los habitantes del territorio nacional a acceder a la información relativa a asuntos ambientales que repercuten de manera directa sobre sus vidas así como la posibilidad de participar en las actividades que les afecten en la temática en cuestión.

El diputado **Pardo** para consensuar una redacción sugiere reemplazar la frase; “esto con el objeto de resguardar el derecho de los habitantes del territorio nacional a acceder a la información relativa a asuntos ambientales que repercuten de manera directa sobre sus vidas así como la posibilidad de participar en las actividades que les afecten en la temática en cuestión” por la siguiente: “La Comisión apoya que el Estado de Chile suscriba este acuerdo, esto con el objeto de resguardar el derecho de los habitantes del territorio nacional a acceder a la información relativa a asuntos ambientales que repercuten de manera directa sobre sus vidas, así como la posibilidad de participar en las actividades que les afecten en la temática en cuestión, sin perjuicio de las reservas que sean conveniente al interés público nacional”.

La recomendación N° 21 propuesta, se somete a votación conjunta, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

RECOMENDACIONES N°s 22 y 23.

Se acuerda votarlas en conjunto

Las recomendaciones propuestas, se somete a votación conjunta, siendo aprobadas en los mismos términos por unanimidad con los votos de los diputados Flores, Ibáñez, Kast, Labra, Longton, Marzán, Pardo, y Verdessi.

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En consecuencia, el texto de las conclusiones y proposiciones APROBADAS por esta Comisión Especial Investigadora es el siguiente:

"CONCLUSIONES:
I.- Responsabilidades.

1.-La investigación que ha realizado la presente Comisión, se funda a partir del mandato de la Sala de la H. Cámara de Diputados, la cual ha sido impulsada por la representación de la Contraloría General de la República al Plan de Descontaminación Atmosférica para Concón, Quintero y Puchuncaví, razón por la cual hasta la fecha estas comunidades se encuentran sin un instrumento para regular la grave contaminación que sufren por material particulado 10 y 2,5, así como también por la emergencia ambiental ocurrida desde el pasado 20 de agosto del 2018 y cuyos responsables hasta hoy no están definidos con total certeza. Sin embargo, la emergencia ha permitido evidenciar un conjunto de acciones y omisiones por parte de las los diferentes poderes y aparatos del Estado, lo que ha generado como consecuencia, que desde que se fundó el parque industrial de Quintero y Puchuncaví, se hayan producido profundos y sistemáticos problemas ambientales. Aquellos se han mantenido sin solución por las diferentes autoridades políticas y administrativas de turno, evidenciándose diferentes tipos y niveles de responsabilidad.

II.- Responsabilidad sobre el Plan de Descontaminación Atmosférica para las comunas Concón, Quintero y Puchuncaví.

2.-La Comisión Investigadora ha logrado consensuar que las responsabilidades políticas en relación al fallido plan de descontaminación atmosférica para la zona, se concentran en el Ministerio del Medio Ambiente, representado para estos efectos, por los ex Ministros Pablo Badenier Martínez y Marcelo Mena Carrasco, con sus respectivos subsecretarios Marcelo Mena Carrasco, Cristián Gutiérrez Pangui, Jorge Canals de la Puente y los jefes de la División de Calidad del Aire, Germán Oyola Fuentes y Andrés Pica Téllez.

3.-El plan de descontaminación atmosférica para las zonas de Quintero y Puchuncaví, fue representado por la Contraloría General de la República, en diciembre del año 2017, por no ajustarse a derecho, toda vez que *"[l]as medidas dispuestas para las aludidas fuentes puntuales, diseñadas sobre la base de esos niveles que son mayores a la real contribución de emisiones por parte de ellas, no se traducen en una efectiva reducción de los contaminantes de que se trata, por lo que el presente instrumento de gestión ambiental no cumple con la finalidad que la normativa le asigna".*

La elaboración del plan de descontaminación atmosférica y por tanto la decisión de confeccionar un inventario de emisiones superior al que correspondía según la Contraloría General de la República, fue realizada durante la gestión del ex Ministro de Medio Ambiente Pablo Badenier Martínez. Si bien, tanto él, como el jefe de la División de Calidad del Aire a su cargo, defienden la metodología como legítima, señalando que fue resultado de un análisis técnico y no de presiones políticas, esta Comisión comparte el criterio de la Contraloría General de la República en cuanto a que tanto el inventario de emisiones contenido en el plan representado y, las medidas de descontaminación que se construyeron a partir de este, no permitían que el plan cumpliera con su objetivo legal.

4.-El proceso de revisión de las observaciones que hizo la Contraloría General de la República se realizaron durante la gestión del ex Ministro de Medio Ambiente Marcelo Mena Carrasco, y por tanto, la decisión técnica y política de no subsanar las observaciones al inventario de emisiones y a las medidas propuestas para emisiones de calderas, fue de dicho Ministro. Su responsabilidad política se acrecienta aún más al comprobar que una vez que se rechazó el plan de descontaminación atmosférica, en diciembre del año 2017, no se hizo absolutamente nada por enmendar los errores, aun cuando en una sesión de la Comisión de Medio Ambiente de la Cámara de Diputados celebrada en enero del 2018, el ex Ministro Marcelo Mena Carrasco se comprometió a enmendar los errores para que estuviera listo antes del término del gobierno de la ex Presidenta Michelle Bachelet.

Asimismo, su responsabilidad fue reconocida por el propio ex Ministro de Medio Ambiente Pablo Badenier Martínez, quien señaló textual en su exposición ante esta Comisión: *"Reconozco que estas observaciones eran subsanables en el trámite de toma de razón ante la Contraloría, desconozco por qué no fueron subsanadas y si no era posible subsanarlas, si yo hubiera sido Ministro, retiro el plan de Contraloría y lo presento al Consejo de Ministros para la Sustentabilidad con las correcciones que me hizo la Contraloría".* Es decir, existiendo todas las posibilidades para subsanar los reparos y observaciones y, así, permitir contar con un plan de descontaminación atmosférica vigente para la zona, el ex Ministro Marcelo Mena Carrasco optó por no hacer nada, lo cual implica una manifiesta falta a sus responsabilidades como Ministro de Estado.

Recordemos que el artículo 70, letra n), de la ley N° 19.300, sobre Bases Generales del Medio Ambiente mandata al Ministro de la Cartera la coordinación del proceso de generación de las normas de calidad ambiental, de emisión y de planes de prevención y, o descontaminación, determinando los programas para su cumplimiento.

Además, para esta Comisión resulta inaceptable que el ex Ministro de Medio Ambiente Marcelo Mena Carrasco no haya asistido a esta instancia en ninguna de las ocasiones en que fue requerido, lo que deja en evidencia la negligencia en su actuación, en atención a la importancia de lo que se investigaba y el rol que jugó. Esto deja de manifiesto su falta de compromiso con la situación que aqueja a la zona, que sólo viene a confirmar el modo de actuar que tuvo cuando fue Ministro de Estado. Por lo demás, tampoco dio respuesta a las preguntas que se le realizaron por escrito por la Comisión Investigadora.

5.-De lo informado por diversos invitados se concluye que en este proceso de revisión de observaciones al plan de descontaminación atmosférica, no se involucró a la SEREMI de Medio Ambiente de Valparaíso a pesar de su participación activa en etapas anteriores de la elaboración del anteproyecto del plan.

6.-Las diferencias entre el inventario de emisiones que llevó a la representación del plan con el inventario basado en emisiones reales, producía un beneficio a la empresas más contaminantes del parque industrial, dándoles mayor holgura de emisión, en detrimento de la comunidad que no se vería beneficiada por una disminución real en la contaminación. En detalle, a AES Gener se le permitía holgura para emitir más toneladas de los tres contaminantes, a CODELCO más dióxido de azufre (SO2) y a ENAP más óxidos de nitrógeno (NOx).

7.-Pese a todo lo señalado**,** nuestro ordenamiento jurídico es insuficiente para perseguir faltas administrativas que pudieran implicar sanciones ante los hechos constatados. Lo anterior se presenta aún más complejo considerando que los plazos para abrir procesos administrativos han caducado. Sin perjuicio de existir una eventual infracción por parte del ex ministro Marcelo Mena Carrasco al artículo 52 N° 2, letra b), de la Constitución Política de la República, al no responder oportunamente las observaciones de la Contraloría General de la República formuladas al plan de descontaminación representado. Así se constata que nuestro ordenamiento jurídico es débil e insuficiente para sancionar faltas administrativas e infracciones legales por parte de las autoridades responsables del medioambiente.

8.-Respecto al instrumento mismo, el proyecto del plan de descontaminación atmosférica señalaba que "*La reducción de emisiones generará los siguiente beneficios: reducción de los casos de mortalidad; reducción de efectos en la salud humana con la consecuente disminución de costos en salud. Adicionalmente, la reducción de MP posee otros beneficios no cuantificados en este análisis como mejora en la visibilidad, disminución de efectos negativos en ecosistemas y mejoras en la vulnerabilidad ambiental de la zona, entre otro*s", en específico, cuantificaba los siguientes beneficios:

Tabla 1: Casos evitados de mortalidad - Plan (2017-2030)

Evento	**Casos evitados 2017-2030 (percentil 50)**			
	Escenario 1	**Escenario 2**	**Escenario 3**	**Escenario 4**
Mortalidad	45	75	64	100
Admisiones hospitalarias	50	83	68	106
Visitas a salas de emergencia	698	1.177	1.013	1.592
Productividad perdida (días)	105.987	177.274	152.553	238.786

Si bien se constata que la sola existencia del plan de descontaminación atmosférica no era suficiente para evitar los episodios de intoxicaciones que se vivieron, es la opinión de esta Comisión que su vigencia de forma integral podría haber contribuido, ya que su principal aporte era precisamente establecer límites a las emisiones de dióxido de azufre, material particulado y óxidos de nitrógeno provenientes principalmente de las empresas AES Gener, Codelco Ventanas y ENAP.

En este sentido, se valora el esfuerzo realizado por el gobierno actual para impulsar con urgencia el nuevo plan dado la presión desatada por el malestar de la comunidad local. Así consideramos positivo que el gobierno haya procesado este instrumento medioambiental, cuya toma de razón se encuentra pendiente por la Contraloría General de la República, como parte de las medidas adoptadas para entregar una solución a los problemas de contaminación ambiental que afectan a la zona. Dicho plan se elaboró en un plazo de tres meses, del cual más del 50% del tiempo fue dedicado al proceso de participación ciudadana, que en 30 días logró una participación de 431 personas, en comparación a las 169 que participaron en PAC del año 2016 en un plazo de 60 días.

Sin embargo, el plan de descontaminación atmosférica es una herramienta insuficiente para hacerse cargo por sí sola de la contaminación que afecta a la zona por más de 50 años. Esto porque tiene como objetivo dar cumplimiento a normas de calidad del aire, las que tienen estándares insuficientes (laxas y permisivas), y de ajustarse a los estándares propuestos por las organizaciones internacionales como la Organización Mundial de la Salud, los beneficios serían aún mayores. Además, la situación de contaminación en la zona se produce por muchos más factores que el incumplimiento de la normativa de aire, así existe contaminación también en suelos y aguas, lo cual tiene que ver con una debilidad institucional de Estado de Chile en materia de medio ambiente y salud de las personas.

III.- Emergencia ambiental en Quintero y Puchuncaví.

9.-La grave crisis ambiental y social vivida en la zona de Quintero y Puchuncaví es el reflejo de un fracaso sistemático del Estado como garante del derecho a vivir en un medio ambiente libre de contaminación tomando en consideración las medidas que se han adoptado en los últimos 50 años, que por cierto, no es posible atribuir a un gobierno en particular. Resulta evidente la falla para establecer políticas eficaces de descontaminación, así como en el objetivo de lograr un acceso al sistema de salud acorde a la situación de los habitantes de la zona. Muy por el contrario, nos encontramos ante un Estado que ha privilegiado consolidar la instalación de empresas contaminantes. En este sentido, es imposible, no atribuir una responsabilidad al Estado de Chile por una evidente falta de servicio histórica en la zona, lo que se ve reflejado en omisiones y acciones tardías en la protección de la salud de las personas y el medio ambiente. No debemos olvidar que la propia Constitución Política prescribe en su artículo 6º, el deber de los Órganos del Estado de someter su acción a la Constitución y a las normas dictadas conforme a ella y garantizar el orden institucional de la República y en el artículo 19 garantiza a todas las personas, en su número 8 el derecho a vivir en un medio ambiente libre de contaminación y en el número 26 la no afectación de la esencia de sus derechos, esto, en relación con el numeral 8, ya referido.

En este sentido, se considera que el conflicto sanitario y medioambiental histórico que afecta a las comunas de Quintero y Puchuncaví no ha sido abordado correctamente por las autoridades competentes en el tiempo. Los daños ocasionados a la población afectada se transforman en previsibles y evitables, cuando los episodios contaminantes se repiten en el tiempo, aumentando su intensidad. Cómo ejemplos se puede enumerar algunos hechos cubiertos por la prensa regional y nacional:

-Nueva intoxicación de alumnos y profesores en La Greda vuelve a poner en la mira las faenas de Codelco Ventanas (El Mostrador - 24 de noviembre de 2011)

-Derrame de 3.000 litros de petróleo se registró en la bahía de Quintero (Cooperativa.cl - 24 de septiembre de 2014)

-Activan planes de contingencia por nuevo derrame de petróleo en la bahía de Quintero (Biobíochile.cl - 13 de agosto de 2015)

-Armada demorará al menos una semana en retirar aceite vertido por ENAP en Quintero (Emol - 17 de mayo de 2016)

-19 alumnos intoxicados por posible emanación de gas (La Estrella Valparaíso - 23 de marzo de 2017)

-Suman nueva investigación en Ventanas por fuerte olor a gas (El Mercurio de Valparaíso - 7 de abril de 2017)

El hecho que las autoridades no ofrezcan a los habitantes afectados un resultado positivo y oportuno, revela la insuficiencia e incapacidad del Estado de Chile y la falta de voluntad política de los gobiernos de turno para hacer frente a lo que estaban llamados precisamente a evitar, prevenir y resolver.

10.-La Comisión Investigadora del año 2011 por la nube tóxica que afectó a la escuela La Greda, permitió poner en evidencia un conjunto de condiciones y elementos que llevaron a las comunas de Quintero, Puchuncaví y Concón a contar con altos niveles de contaminación en aire, agua y suelo. En ese entonces la Comisión presentó un conjunto de recomendaciones para que el Estado tomará medidas y así evitar futuros episodios, sin embargo, pocas de estas recomendaciones, sólo un 17%, fueron tomadas en cuenta y siete años después, nos encontramos nuevamente con una emergencia ambiental que afecta principalmente a niñas, niños y adolescentes, su salud y sus derechos.

En efecto, no se tomaron en cuenta propuestas como: la dictación de normas para aire, suelos y aguas; la dictación de planes de descontaminación para suelos y agua; la destinación de un fondo de salud a las personas afectadas en la zona, la compensación para familiares de quienes hayan perdido la vida en las faenas; exámenes a los habitantes de las zonas más contaminadas, los que debían ser realizados en forma periódica y aleatoriamente, el aseo a las escuelas que debía ser repetido anualmente, por mencionar algunas.

11.-En cuanto al rol que le corresponde a la Cámara de Diputados respecto a las recomendaciones efectuadas por la Comisión investigadora del año 2011, se evidencia la continuidad y profundización de los daños al medio ambiente y a la salud de la comunidad, con eventos de contaminación que han seguido sucediendo desde esa fecha, lo cual demuestra al menos una responsabilidad política de esta Corporación en el seguimiento de las recomendaciones que emanaron del trabajo de la Comisión investigadora del año 2011. El resultado del trabajo de estas comisiones debe ser un insumo técnico y político importante para las labores legislativas y fiscalizadoras de esta Cámara, el cual no se debe descuidar, menos aun cuando está en juego la salud y la vida de las comunidades.

12.-Sin duda existe una responsabilidad del Estado de Chile de no planificar y ejecutar políticas públicas que pudieran prevenir, frenar o resolver el creciente proceso contaminación, al cual se encuentra expuesta las comunidades y el medio ambiente de las zonas afectadas. De la labor realizada por esta Comisión se pueden establecer responsabilidades particulares de las distintas autoridades competentes y en los distintos niveles y sectores del Estado. Sin embargo, también se evidencia una debilidad institucional transversal para hacerse cargo tanto de la prevención como de la gestión de una emergencia de estas características, identificando una falta de herramientas por parte del Ministerio del Medio Ambiente para liderar una evolución del Estado en este sentido.

13.- En materia de prevención y gestión de la emergencia, desde el comienzo de los episodios de contaminación, el gobierno central y regional no tuvieron recursos humanos, jurídicos, ni tecnológicos, ni la capacidad de gestionar una respuesta ante la crisis ambiental. Lo anterior debido a que en Chile no existe un plan de emergencia y de respuesta frente a catástrofes ambientales (como sí lo hay para terremoto, tsunami y otros). La ausencia de estos planes, trajo como consecuencia una actuar errático e insuficiente desde el gobierno, que no permitió

actuar a tiempo y evitar el gran número de intoxicaciones y el daño ambiental que se produjo.

14.- La insuficiente respuesta del Gobierno a la emergencia, sin perjuicio de las responsabilidades políticas particulares, que corresponderían tanto al gobierno regional como al gobierno central, responde principalmente a una debilidad institucional del Estado. Lo anterior permite entender una gestión de la emergencia "a ciegas", toda vez que no se contaba, ni con los instrumentos de gestión ambiental adecuados, ni con equipos de medición y fiscalización suficientes, a pesar de que existieron señales de advertencia como denuncias de las comunidades o estudios solicitados por el propio Ministerio del Medio Ambiente. Por tanto, era esperable que las decisiones de prevención, gestión o incluso sancionatorias, fuesen sin un sustento empírico suficiente. Es así como se evidencia una omisión del Estado en orden a realizar su labor de prevención y control que hubiera permitido que la emergencia no se produjera, o que se produjera en condiciones muy distintas a las ocurridas. Solo recién un mes después de comenzada la emergencia, el gobierno presentó el Decreto de Alerta Sanitaria, a raíz del cual se tomaron las primeras medidas que logran reducir los episodios de contaminación.

15.-En particular, sobre la gestión de la emergencia y ante los antecedentes expuestos, esta Comisión no comparte la decisión de haber suspendido las clases en lugar de haber tomado medidas para disminuir o suspender la actividad industrial que podía originar la contaminación.

16.- Los gobiernos de turno, con los respectivos ministerios y órganos de fiscalización, no han sido capaces de prever y frenar el aumento de la contaminación en las zonas afectadas, muy por el contrario el crecimiento del parque industrial ha continuado y la política pública ambiental, a través de los respectivos instrumentos de gestión, no ha sido suficiente. Sumado a ello, los órganos de fiscalización no han contado con las competencias y recursos para ejercer de forma efectiva, un control sobre el parque industrial.

17.-En este sentido, los instrumentos de gestión ambiental son insuficientes, no permiten ejercer de forma correcta el principio precautorio, toda vez que debe existir un incumplimiento de la normativa (la cual es laxa e insuficiente) para que la Superintendencia de Medio Ambiente pueda tomar medidas preventivas, -lo cual a todas luces carece de sentido-. Junto con ello, una parte importante de las empresas del parque industrial no cuentan con instrumentos de gestión ambiental (Resolución de Calificación Ambiental u otro), lo que no solo impide que dicha Superintendencia pueda sancionar; sino que también, muchas de estas empresas no cuenten con instrumentos que analices y regulen sus emisiones.

18.-Si bien es pertinente señalar que una vez ocurrida la emergencia se realizaron numerosas fiscalizaciones a las empresas que forman parte del parque industrial, estas se produjeron avanzada la emergencia y la crisis ambiental ya era manifiesta. Los mismos representantes de las empresas sostuvieron que las fiscalizaciones realizadas en periodo normal son notablemente más bajas, lo que se conjuga con lo señalado por la Superintendencia de Medio Ambiente y la SEREMI de Salud de la Región de Valparaíso.

19.-En la misma línea, en la Comisión quedó de manifiesto que en materia de fiscalización, la Superintendencia de Medio Ambiente tiene limitadas herramientas y competencias para actuar, dado que su ámbito de acción está restringido a los

mencionados instrumentos de gestión ambiental, (especialmente las RCA) y en el caso de que las empresas no cuenten con estos instrumentos, si bien podría fiscalizar, en ningún caso puede deducir cargos o establecer sanciones, correspondiéndole a la Superintendencia de Electricidad y Combustibles realizar esta labor, con una legislación es aún más laxa y flexible, y por tanto las sanciones son aún más bajas.

20.-Junto con lo anterior, la Superintendencia del Medio Ambiente cuenta con 212 funcionarios a nivel nacional para realizar todas sus competencias y en la Región de Valparaíso para un periodo normal existen tres fiscalizadores. Otro órgano fiscalizador -la SEREMI de Salud-, cuenta también con tres inspectores para fiscalizar la zona afectada. En cuanto a la asignación de recursos, del total de superintendencias que funcionan en la institucionalidad, la de Medio Ambiente está en el penúltimo lugar en materia de presupuestos. La insuficiencia de los recursos queda en evidencia cuando mediante la Res. EX 1545/2018 del Ministerio de Medio Ambiente, se reducen las actividades de fiscalización subprogramadas, para la región de Valparaíso de la Superintendencia de Medio Ambiente, y de otros servicios como subsecretarías y direcciones en materia ambiental, debido a que se tuvo que utilizar recursos adicionales para las fiscalizaciones posteriores a la emergencia.

21.- En materia de instrumentos de medición y estaciones de monitoreo, si bien la autoridad sanitaria – el pasado 23 de noviembre-, entregó las mediciones realizadas con el equipo especial MIRAN XL, que adjudicaban como posible causante de los episodios de contaminación a los hidrocarburos y demás compuestos orgánicos volátiles, hasta el día de hoy no hay total certeza de los componentes que estarían afectando al medio ambiente y a la salud de la comunidad. Lo anterior, porque al momento de comenzar la emergencia no existían en la zona, estaciones de monitoreo o herramientas capaces de detectar los gases que estaban contaminando y las fuentes emisoras de ellos.

En cuanto a los monitores existentes su propiedad y administración se encontraban en manos de empresas contratadas por las mismas industrias que operan en la zona, lo que pone en entredicho la real eficacia y aptitud de dicho sistema de mediciones, sumado esto a la irregularidad de las mediciones con episodios como cortes del suministro eléctrico antes de la emergencia. Todo esto deja en evidencia que no es una buena medida que las propias empresas sean las que administren el monitoreo. Si bien el Estado toma la supervisión directa de las estaciones no toma su administración en forma total, pues estas siguen siendo operadas por la misma empresa contratadas por las industrias de la zona.

22.- La responsabilidad histórica de las autoridades regionales, queda manifiesta al momento de analizar el Plan Regulador Metropolitano del Gran Valparaíso (PREMVAL), cabe destacar que la Comisión Investigadora del 2011 ya había realizado recomendaciones en relación a este punto, las cuales no fueron consideradas. El plan original y sus sucesivas modificaciones, destinaron a Quintero-Puchuncaví como una de las denominadas “zona de sacrificio”, toda vez que permitió que se instalará -y que sucesivamente se expandiera- un sobredimensionado parque industrial. Si bien el plan ha sufrido modificaciones, no ha variado la posibilidad de instalación de proyectos contaminantes, quedando aún disponible 754 hectáreas para su instalación. Como antecedente adicional el 8 de agosto del 2018 -semanas antes del comienzo de la emergencia- la Comisión de Uso del Borde Costero de la Región de Valparaíso, presidida por el Intendente Jorge Martínez Durán, recomendó aprobar a la Subsecretaría de Fuerzas Armadas una modificación de la concesión marítima de la empresa Oxiquim S.A. en la bahía de Quintero, para construir y operar un muelle

mecanizado multipropósito destinado a la transferencia de graneles líquidos y sólidos. Pese a la recomendación unánime de esta Comisión de hacer todos los esfuerzos para no dar curso a la aprobación de este muelle, ante el riesgo de saturar aún más la zona, éste siguió adelante. El Intendente señaló ante esta instancia que todo ese proceso se había realizado de acuerdo a la normativa legal vigente.

Posteriormente se realizó una nueva reunión de la Comisión de Uso del Borde Costero para ratificar el acta, la que fue rechazada por los alcaldes y por los consejeros, sin embargo resultó aprobada con los votos de los funcionarios de gobierno que forman parte de esa Comisión, lo que es responsabilidad del Intendente señor Jorge Martínez Durán.

23.- En materia de legislación, la emergencia evidencia que no ha existido por parte del Estado la voluntad de dictar la normativa necesaria de aire, agua y suelo, que podría haber evitado el conjunto de episodios de contaminación, o que en su defecto hubiera dotado a los órganos de planificación y fiscalizaciones de mayores atribuciones para responder adecuadamente ante la presente crisis ambiental. Cabe agregar, que la necesidad de contar con normas más exigentes es algo que fue recomendado por la Comisión Investigadora del año 2011 y que salvo las siguientes excepciones no fueron atendidas: - establecimiento en el plazo de 3 meses, contados desde la entrada en vigencia del nuevo plan de descontaminación atmosférica, de una oficina de la Superintendencia del Medioambiente, con asiento en Quintero, con dedicación exclusiva a la fiscalización del parque industrial; compromiso establecido en el nuevo PDA para el rediseño y modernización de la red de monitoreo que quedará bajo tuición del estado a contar del segundo semestre; - dictación de nuevas normas de calidad del aire; - implementación de un plan de episodios críticos; - congelamiento de las emisiones, y la incorporación de los COV's , compuesto orgánicos volátiles en el nuevo Plan, entre otras medidas adoptadas con posterioridad a los episodios críticos de agosto.

24.-Uno de los elementos por los cuales se desata la emergencia en la zona, es por la falta de una normativa eficiente y eficaz que impida la emanación de contaminantes, y que establezca procedimientos y sanciones estrictas en caso de incumplimiento. Pues por un lado no todos los gases están normados y los que sí lo están, se miden con parámetros muy por debajo de los estándares internacionales recomendados por las organizaciones internacionales como la Organización Mundial de la Salud. Así, a pesar de que una de las principales hipótesis de los organismos ambientales y de los expertos en salud es que los episodios de emergencia vividos a fines de agosto de 2018 habrían sido causados por emanaciones de compuestos orgánicos volátiles (COV), Chile no cuenta con una normativa de calidad o emisión para estos. Por otra parte, la falta de una norma horaria (o de 10 minutos), para contaminantes como el dióxido de azufre (SO2) permite que durante algunas hora del día se produzcan altas concentraciones de emisión y por tanto, una importante contaminación en la zona -que si bien cumple la normativa vigente- si causa daño a la población y al ecosistema. En este sentido, resulta valorable, el ingreso a la Contraloría General de la república de la Norma Primaria de Calidad de Aire para Dióxido de Azufre, de alcance nacional, que tiene como objetivo proteger la salud de las personas de los efectos agudos y crónicos generados por la exposición a concentraciones en el aire de dióxido de azufre (SO2). Esta nueva norma incorpora de forma inédita el valor de una hora, en línea con lo que ocurre a nivel mundial debido a que los efectos en la salud de este contaminante se evidencian especialmente después de peaks de dióxido de azufre (SO2) de corta duración, muy frecuentes en zonas industriales con presencia de fundiciones de cobre y termoeléctricas a carbón.

Cabe señalar que esta norma se ajustaría a estándares de norma europea mas no se ajustaría a los estándares propuestos por las organizaciones internacionales como la Organización Mundial de la Salud.

25.-La sola existencia de una normativa de aire es completamente insuficiente, toda vez que no se considera de forma completa el ciclo de vida de los contaminantes, ni la formación de nuevos compuestos cuando los gases interactúan entre sí, Ya la Comisión Investigadora del año 2011 señalaba que "*los contaminantes atmosféricos son sólo una arista de este gran problema, eso es evidenciado puesto que a pesar de cumplirse con las normas de calidad de aire en la mayoría de las estaciones de monitoreo, no se ha ponderado la importancia del ciclo de vida completo de dichos contaminantes, que se han depositado desde un inicio en los suelos de Ventanas y sus alrededores*.". Sin embargo los distintos gobiernos han hecho absoluta omisión a la hora de dictar normativa de suelo y agua.

26.-En materia de salud de la población de las zonas afectadas, la omisión y negligencia del Ministerio de Salud y demás autoridades competentes queda manifiesta en palabras de la propia Ministra de Medio Ambiente cuando señala ante esta Comisión: "*Hasta que sucedió esta crisis, el hospital de Quintero ni siquiera contaba con una red de oxígeno".* Lo anterior es especialmente grave en la medida que las zonas en análisis son objeto de un conjunto de políticas públicas por su manifiesta contaminación, sin embargo cuando ocurrió la emergencia, el hospital de Quintero no sólo no contaba con una red de oxígeno, sino que también presentaba múltiples problemas presupuestarios, de falta de personal y de infraestructura adecuada.

27.-Los más de 50 años desde la instalación del parque industrial, sumada a la información entregada por un número importante de invitados a la Comisión, develan que la población de las zonas de Quintero y Puchuncaví, están siendo afectadas gravemente en su salud. La gran cantidad de contaminantes que emanan del parque industrial hacen temer que enfermedades como el cáncer, respiratorias, infartos al miocardio, entre otras pudieran estar afectando a la población. En este sentido, antes del comienzo de la emergencia, no existieron exámenes toxicológicos para la población de la zona afectada, ni menos un catastro con información toxicológica. La autoridad sanitaria no ha sido clara a la hora de determinar cuáles son los límites de tolerancia de las personas respectos a estos agentes tóxicos y por tanto, existe un temor fundado que las enfermedades mencionadas -de creciente aumento en la población de la zonas- pudieran encontrar su causa en la contaminación medioambiental y por tanto estar causando la muerte de muchos habitantes de Quintero y Puchuncaví.

28.- La Comisión Investigadora del año 2011, destacó entre sus conclusiones, el incumplimiento de las obligaciones del Estado respecto del derecho a vivir en un ambiente libre de contaminación. Después de siete años de aquella declaración, esta Comisión concluye que el conjunto de omisiones del Estado de Chile en materia medio ambiental, no tan solo constituyen una vulneración del Estado al derecho a vivir en un ambiente libre de contaminación, pues debido al aumento de la crisis ambiental en las zonas afectadas, hoy podemos hablar de un conjunto de violaciones de derechos fundamentales de los habitantes de la zona de Quintero y Puchuncaví, quienes han sido vulnerados en su derecho a la vida, derecho a la salud, derecho a la educación. Lo anterior es una responsabilidad conjunta de los distintos gobiernos de turno, a escala central y local.

IV.- Responsabilidad de las empresas del parque industrial.

29.-Los diferentes representantes de las empresas que asistieron a la Comisión manifestaron que todas las unidades cumplen con la normativa medio ambiental y que las irregularidades detectadas en su funcionamiento tendrían el carácter de excepcional, no pudiendo concluirse que aquellas sean las causantes de la contaminación. Sin embargo, la autoridad sanitaria y medio ambiental, desde el comienzo de la emergencia ha realizado un conjunto de fiscalizaciones, que si bien no permiten tener certeza respecto a las emisiones contaminantes y delas empresas responsables, si comienzan a delinear un conjunto de irregularidades que pudieran conducir a establecer responsabilidades en la emergencia.

En la línea de las fiscalizaciones, los sumarios cursados contra empresas como: ENAP (problemas en la actividad de mantención de los estanques T5104 y T5109), GNL Quintero (fallas en la estación de monitoreo de calidad de aire -Centro Quintero-), OXIQUIM (utilización de los estanques 306 y 307 para almacenamiento de sustancias distintas a las autorizadas), entre otras, son reflejo de lo planteado. Junto con ello, el 17 de diciembre el Seremi de salud daba cuenta a la Comisión de la existencia de 21 sumarios sanitarios cursados dentro de los cuales destaca el realizado a la empresa ENAP y ENEX, por el incumplimiento de los planes operacionales que las mismas empresas confeccionaron.

30.- Si bien en general las empresas han dado cumplimiento a la normativa de emisiones, la falta de certeza en cuanto a las responsabilidades por la emergencia ambiental, plantea la necesidad de elevar el estándar en que analizamos la contaminación de la zona. El cumplimiento de una normativa laxa, insuficiente y permisiva, no es suficiente para paliar las negativas consecuencias que producen los agentes contaminantes en la población. Los episodios vividos durante el año 2018, ponen de manifiesto la poca inversión y gestión de las empresas en adquirir tecnología suficiente, que les permita contar con las herramientas necesarias para disminuir la cantidad de contaminación que atenta no sólo contra la población que habita en los alrededores de sus plantas, sino contra todo el ecosistema de la zona.

31.-El Estado de Chile -como dueño de CODELCO y de ENAP-, es un responsable directo de la contaminación histórica que yace en la Bahía de Quintero y Puchuncaví, y que afecta a sus habitantes, pero esta responsabilidad radica no solo en las emisiones de estas empresas, sino que también por haber autorizado la instalación de las diferentes unidades industriales en la zona, ninguna de las cuales ha asumido su responsabilidad histórica por la contaminación.

32.-Respecto a los trabajadores del conjunto de empresas que componen el parque industrial, los diversos invitados -representantes de los trabajadores y de las comunidades-, señalaron que no hay certeza respecto de que se están tomando las medidas pertinentes, por las diferentes empresas, para evitar enfermedades como el cáncer y las cardio-respiratorias o para prevenir accidentes laborales.

33.- Si bien -a la fecha- ninguna de las fiscalizaciones y sumarios cursados, ha podido determinar con certeza alguna responsabilidad directa de las empresas en los episodios de contaminación, queda claro que todas las empresas del parque industrial contribuyen a la contaminación. Sumado a ello, una gran parte de estas industrias están siendo objeto de fiscalizaciones y sumarios que se encuentran en curso, constatándose múltiples irregularidades.

34.-En conclusión, debido a las deficiencias normativas, institucionales y de infraestructura, parece ser imposible detectar con exactitud qué compuesto está contaminando y de qué empresa proviene, pues la: (i) la existencia de varios contaminante, (ii) las estaciones de monitoreo que solo miden los gases normados, (ii) el fenómeno de los peaks de emisiones, (iv) las condiciones meteorológicas y de ventilación, entre otros factores, hacen que al día de hoy no tengamos certezas. A esto se le debe sumar que la institucionalidad ambiental vigente hace difícil establecer una relación de causalidad entre los efectos de la contaminación y los responsables de esta. Sin embargo, a pesar de las debilidades institucionales, la Comisión adquiere la convicción que la responsabilidad por la contaminación de la zona de Quintero Puchuncaví, encuentra su causa directa en las emisiones de las empresas que conforman el parque industrial asentado en la zona; donde, debido a décadas de omisiones y negligencias del Estado de Chile, instalaciones industriales, privadas y estatales, han sobreexplotado y contaminado la zona, trayendo devastadores consecuencias para la población y el medio ambiente. Por ello, además se considera imprescindible contar con una mejor regulación de aquellas industrias cuyo aporte porcentual concentra más del 75% de las emisiones en material particulado, dióxido de nitrógeno (NOx) y dióxido de azufre (SO2), como son Codelco Ventanas, Gener Ventanas y Enap Aconcagua

V.-De las denominadas zonas de sacrificio.

35.-La revisión de los antecedentes por esta Comisión, de otras de las denominadas zonas de sacrificio a saber, Coronel, Huasco, Mejillones y Tocopilla, permite identificar elementos comunes ya descritos para Quintero y Puchuncaví. En aspectos generales, se identifican como causantes de la situación de contaminación la actividad industrial desregulada, tanto en su instalación como en su operación, que no ha sido prevenida por los instrumentos de ordenamiento territorial, ni las normas de calidad y emisión, ni la institucionalidad ambiental como la superintendencia o el sistema de evaluación de impacto ambiental. En aspectos específicos, destaca la cercanía de las instalaciones industriales con las viviendas, escuelas y liceos, lo que se ve reflejado en altos niveles de contaminación por metales pesados de estas instalaciones en sus techos, entretechos, patios y otras superficies.

36.- La generación eléctrica a partir de carbón, sus instalaciones y actividades asociadas con el transporte de carbón y residuos, vertederos de cenizas, emisiones de material particulado, entre otros, es un factor común a las denominadas zonas de sacrificio analizadas en esta comisión. 27 de las 29 termoeléctricas a carbón en funcionamiento en Chile se encuentran emplazadas en estas denominadas zonas de sacrificio, existiendo 7 con más de 40 años de antigüedad. Estas son responsables de gran parte de la contaminación de estas zonas, sobre todo por material particulado y metales pesados. Constatar el hecho que las termoeléctricas de nuestro país se encuentren concentradas en 5 comunas, refuerza la idea de que estas comunidades están siendo sacrificadas en pos de la generación eléctrica del país, de las cuales las termoeléctricas representan el 21% de la matriz, de acuerdo al anuario estadístico de energía del año 2017.

37.- Esta Comisión constata que la concentración territorial que ocurre en particular con las termoeléctricas, ocurre con la industria general en las denominadas zonas de sacrificio. Esto da cuenta que el Estado ha fallado en distribuir de forma equitativa los costos e impactos del crecimiento industrial, otorgando mayor carga a unos territorios y sus comunidades por sobre otras. Es necesario implementar medidas efectivas para revertir esta situación y para evitar que otros territorios y

comunidades sean sacrificados por la instalación de proyectos con impacto ambientales intolerables para el contexto local.

38.- Otro efecto común presente en las denominadas zonas de sacrificio, es la incompatibilidad de la actividad industrial con otras actividades productivas que se ven afectadas por causa de la contaminación, como la agricultura, turismo o pesca. Esta última, generalmente es la pesca artesanal, dependiente del estado de las aguas y fondos marinos, las más afectadas en estas comunidades costeras.

39.- Dentro de los efectos sobre la salud, destacan como elementos comunes a las denominadas zonas de sacrificio los problemas asociados a necesidades educativas especiales (autismo, déficit atencional, entre otros), enfermedades respiratorias y la mayor prevalencia de cáncer en la población.

40.- Las comunidades de las denominadas zonas de sacrificio dan cuenta de que los mecanismos de participación ciudadana sobre decisiones relevantes para el desarrollo en sus territorios no son efectivos y de una asimetría de información entre los titulares de proyectos y las comunidades, lo que no permiten que se integren de manera adecuada a la toma de decisiones.

41.- Se reconoce que las denominadas zonas de sacrificio son territorios especialmente vulnerables ante el cambio climático y por lo tanto requieren atención especial para mitigar sus efectos locales. Esto considerando factores como su ubicación costera o la contaminación de aguas disponibles para riego o consumo humano.

42.- Tal como consta en la presentación ante esta Comisión del ex jefe de la División de la Calidad del Aire del Ministerio de Medio Ambiente, Germán Oyola, el plan de prevención atmosférica de Huasco cuenta con un inventario de emisiones construido bajo la misma metodología que el plan para Quintero y Puchuncaví representado por la Contraloría General de la República, sin embargo el plan de Huasco fue aprobado. Se debe hacer presente que los antecedentes recabados por esta Comisión no dan cuenta de la diferencia de criterios.

43.- Finalmente esta Comisión Investigadora hace presente su descontento ante la escasa colaboración de algunos Órganos del Estado, de la Administración del Estado, autoridades y exautoridades de gobierno o municipales, por la poca celeridad en responder oficios de importancia para el cumplimiento del objetivo de la Comisión. Resultaba de especial relevancia el compromiso de los Órganos Públicos para contribuir en el desarrollo de la labor de la Comisión Investigadora en orden a esclarecer puntos controvertidos. Sin ir más lejos, aún hay oficios sin responder y otros que fueron respondidos fuera de plazo, lo que demuestra la exigua disposición de algunos a colaborar.

En específico, referente a lo precitado, los órganos y oficios en dicho estado se encuentran:

- Oficios cuyas respuestas excedieron de 30 días dirigidos: la Ministra del Medio Ambiente, señora Carolina Schmidt; al Ministro del Interior señor Andrés Chadwick; al Director Nacional de ONEMI, señor Ricardo Toro; al Intendente Regional de Valparaíso, señor Jorge Martínez; a la Gobernadora de Valparaíso, señora María de Los Ángeles de la Paz Riveros; a la Seremi de Medio Ambiente, señora María Victoria Gazmuri; al Superintendente de Electricidad y Combustible, señor Luis Ávila;

al Superintendente del Medio Ambiente; al Alcalde de Quintero, señor Mauricio Carrasco; a la Alcaldesa de Puchuncaví, señora Eliana Olmos, y al Alcalde de Concón, señor Oscar Sumonte.

- Oficios no respondidos por: el Ministro de Salud, señor Emilio Santelices; el Ministro de Obras Públicas, señor Juan Fontaine; la Ministra del Medio Ambiente, señora Carolina Schmidt; el Ministro de Hacienda, señor Felipe Larraín; el Contralor General de la República, señor Jorge Bermúdez; el Subsecretario para Fuerzas Armadas, señor Juan Galli; la Directora de Sernapesca, señora Alicia Gallardo; el Director del Servicio de Evaluación Ambiental, señor Hernán Brücher; el Director General Policía de Investigaciones de Chile, señor Héctor Espinosa; el Gobernador Marítimo de Valparaíso, señor Juan Gajardo; la Alcaldesa de Puchuncaví, señora Eliana Olmos; el Alcalde de Quintero, señor Mauricio Carrasco; el ex Ministro y ex Subsecretario de Medio Ambiente, señor Marcelo Mena Carrasco, y el ex jefe de la División de la calidad del Aire del Ministerio de Medio Ambiente, señor Germán Oyola.

RECOMENDACIONES:

1.- Generación de un Plan de Emergencia para catástrofes ambientales y químicas, que active una serie de mecanismos para una actuación rápida y eficaz de los Órganos de Estado. La generación de este plan debe permitir convocar y coordinar a las diferentes entidades implicadas en la institucionalidad ambiental y laboral, con el objeto de establecer medidas de prevención, mitigación y preparación ante potenciales emergencias químicas, y planes de respuesta en caso de que ocurra el evento; considerando tanto capacidades establecidas en las instituciones, como la infraestructura e insumos. Dentro de este plan se debe contemplar un sistema de alarma preventiva, gestión de la emergencia, fondos de salud y recuperación de ecosistema. Este plan se debiera construir en conjunto con las comunidades y sus organizaciones. Sin perjuicio de la incorporación de la gestión de episodios críticos en el nuevo PDA, se constata la necesidad de contar con la nueva institucionalidad de la ONEMI a objeto de que esta entidad pueda ejercer un rol preponderante en la coordinación de la respuesta y apoyo en casos de emergencia ambiental.

2.- Llevar a cabo a la brevedad, **las mediciones de contaminantes en aire, suelo y aguas** -de consumo humano, proveniente de los servicios de agua potable de la zona o de pozo, así como de las aguas marítimas que bordean la bahía de Quintero-, enmarcándolas en los más altos estándares internacionales prescritos por las organizaciones internacionales como la Organización Mundial de la Salud; y asegurando que en dichos procedimientos de medición participen representantes de la sociedad civil, de modo de mitigar la desconfianza generalizada que actualmente existe en la zona.

3.- Que, el Instituto de Salud Pública, realice de manera **planificada y gratuita los exámenes toxicológicos** necesarios que permitan determinar con **certeza e imparcialidad**, la existencia o no, de contaminantes en el cuerpo de los habitantes de las denominadas zonas de sacrificio (sangre, orina o metabolitos), esto, con el fin de garantizar el acceso a los tratamientos médicos que permitan detener el deterioro de su estado de salud física y psíquica, como asimismo establecer la asociación entre éstos y las fuentes contaminantes que permitan a posteriori, establecer las responsabilidades al respecto.

4.-Que, se ordene y habilite a los Servicios de Salud de las denominadas zonas de sacrificio, **la implementación de un sistema de monitoreo permanente,**

efectivo y veraz, respecto del estado de salud de los habitantes de la zona y su potencial afectación a largo plazo, con el fin de mantener un registro actualizado del estado de salud de la población.

5.-La inmediata elaboración de la Ley Especial para las denominadas zonas de sacrificio con la participación de la sociedad civil, contemplando demandas trabajadas en los últimos 3 años. Se trataría de una ley que reconoce la contaminación, el daño sobre la comunidad y propone medidas de reparación y compensación, como becas para estudios, subsidios de vivienda, controles de salud, entre otros, similar a lo implementado por la Ley de Polimetales de Arica, pero considerando las particularidades de cada territorio y comunidades afectadas.

6.-En cuanto a las estaciones de monitoreo, se propone que pasen a propiedad, administración y gestión del Ministerio de Medio Ambiente y que sean incluidas dentro de la Red Nacional de Monitoreo de Calidad del Aire. Es fundamental generar un sistema de monitoreos que sea (i) interconectado entre las distintas estaciones, (ii) con estándares internacionales para certificar la calidad real del aire en la zona, (iii) que mida todo tipo de gases, incluso aquellos que no se encuentran normados y respecto de los cuales exista peligro de que puedan contaminar. Además de considerar necesario el aumento del número de estaciones, también se debe exigir el mantenimiento, calibración y certificación de los equipos de monitoreo por instituciones externas debidamente calificadas, sin vinculación alguna con las empresas emisoras de contaminantes.

7.-Se debe modificar, a la brevedad, los actuales instrumentos que rigen el ordenamiento territorial de la zona -el Plan Regulador Metropolitano de Valparaíso- y congelar las autorizaciones de inversión en las 754 hectáreas aún disponibles para actividades industriales peligrosas. Junto con ello, es fundamental un cambio en el uso de suelo, de forma tal que dichos espacios sean ocupados con un fin distinto al industrial y permitan paralizar de forma indefinida la presentación de proyectos que busquen aumentar la densidad del parque industrial.

8.-Paralización inmediata y en forma indefinida de todos los proyectos y permisos que se hayan otorgado o estén en curso, por parte de las autoridades competentes, para nuevas concesiones en la Bahía de Quintero.

9.-Fortalecer la Evaluación Ambiental Estratégica como herramienta para incorporar factores ambientales a la evaluación de instrumentos de planificación territorial, haciendo sus conclusiones vinculantes para la elaboración de estos.

10.- Homologación de la normativa de aire (material particulado y sus precursores) con los estándares internacionales establecidos por la las organizaciones internacionales como la Organización Mundial de la Salud. En específico, la modificación de las normas primarias de calidad del aire para el dióxido de azufre (SO_2) contemplando una norma horaria y también una norma especial de diez minutos para casos de alerta preventiva de emergencia ambiental. Ambas normas deben ser homólogas a las recomendadas por las organizaciones internacionales como la Organización Mundial de la Salud.

11.- Es imperioso que el Ministerio de Medio Ambiente revise y actualice a la brevedad el DS N° 28, que establece norma de emisión para fundiciones de cobre y fuentes emisoras de arsénico y dicte normas complementarias, para que se establezcan estrictas regulaciones a emisiones de contaminantes críticos o de alto

riesgo para la población como el mercurio y arsénico, entre otros que se producen en fundiciones y termoeléctricas.

12.- De igual manera, se deben dictar normas de calidad y emisión relativas a los metales pesados, originados por la actividad industrial, en particular por el uso del carbón. Así mismo se deben dictar normas de calidad y emisión de compuestos orgánicos volátiles, considerando que pueden ser los eventuales causantes de las intoxicaciones producidas en Quintero y Puchuncaví. Estas normas deben contemplar las matrices de aire, agua y suelo, cuando corresponda. De esta forma se podrán establecer planes de descontaminación orientados no solo a la calidad de aire, sino también a la calidad de los suelos y aguas. Las consecuencias de los proyectos de inversión se observan en todos los elementos del ecosistema y es necesario normar y regular el funcionamiento de éstos en todos sus ámbitos.

13.- Elaborar, a la brevedad, normas primarias y secundarias de calidad de los suelos y de aguas, según los estándares recomendados para proteger la salud de las personas y el medioambiente, tomando como referencia la normativa internacional o recomendaciones de organismos internacionales como la Organización Mundial de la Salud o la Organización de las Naciones Unidas para la Alimentación.

14.- Si bien las emisiones de las empresas del parque industrial se deben medir y controlar de forma individual, es fundamental establecer una norma de medición que considere la sumatoria de las emisiones de todas las empresas del parque industrial, reconociendo que la mezcla de las emisiones tiene efectos sinérgicos que afectan a la salud y el medio ambiente de forma distinta a las emisiones individuales. Se propone como política de Estado la introducción de industria descontaminante asociada a los complejos industriales, incorporando la experiencia internacional.

15.- Acelerar el proceso de cierre o conversión de las centrales termoeléctricas a carbón, comenzando por cerrar a la brevedad las siete termoeléctricas con más de 40 años de antigüedad (Tocopilla U12, U13, U14 y U15, Ventanas 1 y 2, Bocamina) para luego dar cierre o conversión a las restantes con el año 2030 como plazo máximo.

16.- Modificar el actual Sistema de Evaluación de Impacto Ambiental (SEIA) de modo que exprese de forma clara los principios precautorio y preventivo, así como también una noción de justicia ambiental. Para esto al menos debe incorporarse mecanismos para contemplar los efectos sinérgicos en la evaluación y evitar la concentración de proyectos contaminantes en un territorio.

17.- Aplicar los cambios regulatorios necesarios para que los proyectos que no cuentan con Resolución de Calificación Ambiental (RCA) y cuyas características de impactos ambientales así lo ameriten, deban someterse al SEIA a la brevedad, de forma de poder determinar y controlar sus impactos ambientales. En paralelo se hace necesario fortalecer la institucionalidad ambiental, especialmente la labor fiscalizadora de la Superintendencia de Medio Ambiente, que debe contar con atribuciones que le permitan no solo velar por el cumplimiento de las RCA de los proyectos, sino también poder fiscalizar empresas y actividades que no cuentan con esta resolución y puedan estar afectando al medio ambiente En particular las empresas más antiguas se encuentran hoy en día desreguladas.

18.- Otorgar más recursos en los próximos Presupuestos de la Nación, al Ministerio del Medio Ambiente, a la Superintendencia de Medio Ambiente y al Servicio de Evaluación Ambiental, para que puedan contar con mayor personal para cumplir con sus labores y con tareas urgentes como las identificadas por esta Comisión, como la actualización de normativa medioambiental, fiscalización, evaluación de proyectos, entre otras.

19.-Tipificar el delito medio ambiental. Se propone un tipo penal que castigue el daño a los componentes del medio ambiente (aire, agua, suelo, vida animal y vegetal), así como el riesgo de contaminación, originados tanto en la acción dolosa como negligente del agente contaminante.

20.-Implemente, a la brevedad, a través del Ministerio de Salud y Medio Ambiente, una campaña de información dirigida a la población de las comunas de Quintero y Puchuncaví, que implique informar de manera oportuna, veraz, confiable y comprensible a todos y cada uno de sus habitantes, acerca del actual estado de la crisis ambiental y sanitaria que afecta a la zona, indicando las causas y sus efectos, las medidas oficiales que se toman y su evaluación, de manera de mitigar la desinformación que existe en la población.

21.-El Estado debe promover las mejores prácticas sobre acceso a la información, participación pública y acceso a la justicia en asuntos ambientales, conforme a los tratados internacionales sobre derechos humanos, en línea con lo establecido en el cuerdo Regional sobre el Acceso a la Información, la Participación Pública, y el Acceso a la Justicia en Asuntos Ambientales en América Latina y el Caribe, conocido como el “Acuerdo de Escazú”. La Comisión apoya que el Estado de Chile suscriba este acuerdo, esto con el objeto de resguardar el derecho de los habitantes del territorio nacional a acceder a la información relativa a asuntos ambientales que repercuten de manera directa sobre sus vidas, así como la posibilidad de participar en las actividades que les afecten en la temática en cuestión, sin perjuicio de las reservas que sean conveniente al interés público nacional.

22.-Es relevante promover mejores prácticas sobre acceso a la información, participación pública y acceso a la justicia en asuntos ambientales conforme a los tratados internacionales sobre derechos humanos. Lo anterior, entendiendo que los problemas ambientales derivados del funcionamiento de proyectos de inversión repercuten directamente sobre la vida de las personas. Es fundamental que las comunidades puedan participar y tener voz en las actividades que afecten su diario vivir.

23.- Exigir a las empresas instaladas en las denominadas zonas de sacrificio, un plan de inversiones para controlar sus emisiones, prohibiendo emisiones fugitivas, de forma tal que les permita adquirir tecnología de punta, pues tal como lo señalaba la Comisión Investigadora del año 011 *“Es evidente que el sólo cumplimiento de las normas actuales no garantiza la calidad ambiental de la zona Puchuncaví-Quintero por el efecto acumulativo histórico de emisiones, por lo cual CODELCO y el resto de las empresas deben asumir acciones urgentes de mitigación, concordadas con las autoridades competentes”.*

Junto con ello, las empresas públicas y privadas del parque industrial deben asegurar el deber de respeto de los derechos humanos de las comunidades en las cuales llevan a cabo sus actividades productivas. Es importante que las empresas localizadas en la zona asuman la necesidad de incorporar en sus políticas

los Principios Rectores sobre las Empresas y Derechos Humanos de Naciones Unidas y los estándares que de ellos se derivan para su actuar, con especial énfasis en el principio operativo N° 17 que hace referencia a que *"las empresas deben proceder con la debida diligencia en materia de derechos humanos"*, con el fin de identificar, prevenir, mitigar y responder de las consecuencias negativas de sus actividades sobre los derechos humanos.

IV.-CONSTANCIAS REGLAMENTARIAS.

A) ENVÍO COPIA DEL INFORME DE LA COMISIÓN INVESTIGADORA.

La Comisión Investigadora acordó proponer a la H. Sala de la Cámara de Diputados que se envíe copia de este informe a las siguientes instituciones públicas, con la finalidad que, de conformidad a su mérito, adopten las medidas conducentes a superar las dificultades detectadas en la investigación de esta comisión parlamentaria.

1) A S.E. El Presidente de la República, de conformidad con las disposiciones del artículo 58 de la ley N° 18.918, Orgánica Constitucional del Congreso Nacional.

2) A la Ministra del Medio Ambiente.

3) Al Ministro de Salud.

4) Al Intendente de la región de Valparaíso, señor Jorge Martínez Durán.

B) DIPUTADO INFORMANTE.

La Comisión Investigadora designó, por unanimidad, como Diputado Informante al señor Diego Ibáñez Cotroneo.

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Tratado y acordado según consta en las actas correspondientes a las sesiones de fechas 5, 10 y 24 de septiembre; 1, 5, 8, 22, 26 y 29 de octubre; 5, 12, 16 y 19 de noviembre; 10, 17, 20 de diciembre de 2018, y 7, 21 y 22 de enero del año en curso, con la asistencia de los diputados miembros de la Comisión señores(as) Diego Ibáñez Cotroneo (Presidente), Camila Flores Oporto, María José Hoffmann Opazo, Pablo Kast Sommerhoff, Amaro Labra Sepúlveda, Andrés Longton Herrera, Carolina Marzán Pinto, Luis Pardo Sáinz, Patricio Rosas Barrientos, Rene Saffirio Espinoza, Marcelo Schilling Rodríguez, Osvaldo Urrutia Soto y Daniel Verdessi Belemmi.

Asistieron, además, los diputados señores Andrés Celis Montt; Marcelo Díaz Díaz en reemplazo del diputado Patricio Rosas Barrientos, José Miguel Castro Bascuñán en reemplazo de Camila Flores Oporto, y los diputados Eduardo Durán Salinas y Karin Luck Urban, ambos en reemplazo del diputado Andrés Longton Herrera.

SALA DE LA COMISIÓN, a 23 de enero de 2019.

CLAUDIA RODRÍGUEZ ANDRADE
Secretaria Abogada de la Comisión

INDH
INSTITUTO NACIONAL DE DERECHOS HUMANOS

70 AÑOS
Declaración Universal de Derechos Humanos

INFORME MISIÓN DE OBSERVACIÓN ZONA DE QUINTERO Y PUCHUNCAVÍ 11 al 13 de septiembre de 2018

Informe aprobado por el Consejo del Instituto Nacional de Derechos Humanos en sesión ordinaria N°446 del 1° de Octubre de 2018

I. Mandato Legal del Instituto Nacional de Derechos Humanos

El Instituto Nacional de Derechos Humanos (INDH) es una corporación autónoma de derecho público creada en virtud de la Ley 20.405, que tiene por objeto la promoción y protección de los derechos humanos de las y los habitantes del territorio nacional y que asienta el cumplimiento de su mandato institucional en los Principios de París, garantizando así, orgánica y funcionalmente su independencia, autonomía y pluralismo.

Sus funciones, son las de promover que la legislación, los reglamentos y las prácticas nacionales se armonicen con los instrumentos internacionales de derechos humanos, a fin que su aplicación sea efectiva.[1] En ese marco se encomienda desarrollar, entre otras acciones, las de comunicar al Gobierno y a los distintos órganos del Estado su opinión respecto de las situaciones relativas a los derechos humanos y proponer a los poderes públicos las medidas que estime deban adoptarse para favorecer la protección y la promoción de los derechos humanos consagrados en las normas constitucionales y legales, en los tratados internacionales suscritos y ratificados por Chile y que se encuentran vigentes, así como en los principios generales de derecho reconocidos por la comunidad internacional. En ese entendido, le corresponde al INDH velar por el ejercicio de los derechos humanos en el país, los cuales pueden resultar vulnerados por diversos actos u omisiones de organismos estatales y/o privados y en ese contexto, está facultado para efectuar Misiones de Observación con el objeto de verificar en terreno posibles vulneraciones de derechos.

II. Antecedentes y mandato de la Misión de Observación

El día 21 de agosto de 2018, durante la jornada de la mañana, habitantes de las comunas de Quintero y Puchuncaví presenciaron -como en ocasiones anteriores- una nube emanada del parque industrial emplazado en el cordón industrial de la zona y percibieron olores molestos. Como resultado, 71 personas -principalmente niños, niñas y adolescentes, profesores y personas mayores- presentaron síntomas de intoxicación por inhalación, las que fueron derivadas a distintos dispositivos de salud de la Región de Valparaíso, principalmente al Hospital Adriana Cousiño de Quintero y al Hospital Gustavo Fricke de Viña del Mar. A raíz de esta situación, la Dirección Regional de ONEMI realizó la evacuación preventiva de 200 estudiantes por incidente con material peligroso en la comuna de Quintero. Además, la SEREMI de Educación suspendió las clases en los establecimientos

[1] Ley 20.405, artículo 3°, numerales 2, 3 y 4.

educacionales, medida que se inició la tarde de ese mismo día y se extendió hasta el miércoles 22 de agosto.[2]

Frente a las denuncias de la ciudadanía sobre la aparición de un polvo de color amarillo en las calles de la zona afectada, el Intendente de Valparaíso, Sr. Jorge Martínez Durán, descartó que "fuese dióxido de azufre, agregando que se trata[ba] de polen caído de los árboles". [3]

El miércoles 23 de agosto, un segundo episodio ocurrido en la zona, sumó más personas afectadas, alcanzando -entre ambos acontecimientos- un total de 133 intoxicaciones por contaminación atmosférica (90 adultos/as y 43 menores de edad).[4]

A propósito de estos hechos, el Intendente de Valparaíso convocó al Comité Operativo de Emergencia[5] (COE) el 24 de agosto y decidió declarar, mediante el Informe Técnico N° 230-A y la Resolución 6300, el estado de alerta amarilla para las comunas de Quintero y Puchuncaví en razón de un incidente por material peligroso, aplicable desde el jueves 23 de agosto y hasta que las condiciones así lo ameritaran, siendo finalmente cancelada el 2 de septiembre.

En base a los Informes Técnicos N°726 y N°727 entregados por la Dirección Regional de ONEMI Valparaíso, el COE indicó que las sustancias tóxicas serían distintas en los dos episodios: en una primera medición fueron detectados Metilcloroformo, Nitrobencenato y Tolueno como contaminantes en la atmósfera; mientras que en el segundo episodio, si bien se confirmó la presencia de materiales peligrosos en el ambiente, no se logró identificarlos en específico, así como tampoco el origen de la emisión.[6] Adicionalmente, por orden del COE, se dispuso la creación de un Hospital de Campaña por parte de la Defensa Civil, al interior del Hospital Adriana Cousiño de Quintero.

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[2] Reporte de incidente por material peligroso, publicado por ONEMI el 21 de agosto de 2018 a las 21:10 horas.

[3] Información indicada en diversos medios de prensa. Véase al respecto "Intendente de Valparaíso confirma que intoxicación se debe a gases de hidrocarburo, y Codelco y Enap descartan responsabilidad". Disponible en http://www.emol.com/noticias/Nacional/2018/08/23/918110/Intendente-de-Valparaiso-confirma-que-incidente-ambiental-fue-generado-por-gases-de-hidrocarburo.html

[4] Reporte de incidente por material peligroso, publicado por ONEMI el 23 de agosto de 2018 a las 19:00 horas.

[5] Creado bajo el Decreto Supremo D.S. N° 38/2011 del Ministerio del Interior. Este Comité se constituye cuando se registran emergencias, desastres o catástrofes que provoquen daños de consideración en las personas y/o los bienes, que afecten todo o parte del territorio nacional –o cuando se vean involucradas dos o más regiones del país-, o bien, en el caso que las afectadas sean una o más comunas de una misma región, y que el Ministro del Interior resuelva que el siniestro provoca un alto impacto en la población.

[6] Reporte de Monitoreo de Alerta Amarilla para las comunas de Quintero y Puchuncaví por incidente por material peligroso, publicado por ONEMI el 24 de agosto de 2018 a las 10:35 horas.

Ese mismo día, el Intendente de Valparaíso, Sr. Jorge Martínez Durán, a través de diversos medios de prensa, aseguró que se tenían "*evidencias concretas que algunas tareas que estaba realizando ENAP en su planta local han generado emisión de contaminantes del tipo que ha causado intoxicación en la zona*".[7] Paralelamente, la Ministra del Medio Ambiente solicitó a la Superintendencia del Medio Ambiente (SMA) paralizar ENAP, ante el riesgo para la salud de la población.[8]

No obstante las medidas tomadas por las autoridades, el día 4 de septiembre un nuevo episodio de contaminación afectó a la comuna de Quintero. De acuerdo con la información proporcionada por la Dirección Regional de ONEMI, 59 alumnos de diversos establecimientos educacionales de la comuna de Quintero, habrían presentaron malestares que se atribuyeron a la presencia de un material desconocido en el ambiente.[9]

Estos recientes episodios de contaminación no son nuevos ni aislados y, en este sentido, el 28 de agosto de este año, el Consejo del INDH emitió una declaración pública en que "manifiesta su preocupación y solidariza con la comunidad de Quintero y Puchuncaví, ante los últimos eventos de contaminación registrados en dicha zona", advierte que "la institucionalidad ambiental debe realizar las investigaciones pertinentes para esclarecer los últimos hechos que han afectado seriamente a la población, adoptando las medidas necesarias para su no repetición y determinando si es el caso las sanciones y otras acciones que en derecho correspondan", agregando además que "si estas investigaciones determinan responsabilidad de empresas en el reciente episodio de contaminación en la zona, proponemos que dichas empresas impulsen procesos de debida diligencia a objeto de evitar la afectación de derechos de la población a futuro y de reparar los daños que puedan haber contribuido a provocar."[10]

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[7] La cita aparece en diversos medios de prensa del día. Véase, por ejemplo, en Radio Biobío, "Gobierno culpa a ENAP por intoxicación en Quintero: "Tenemos evidencias concretas", disponible en https://www.biobiochile.cl/noticias/nacional/chile/2018/08/24/intendente-existen-antecedentes-certeros-para-culpar-a-enap-por-intoxicacion-en-quintero.shtml; Teletrece, "Gobierno responsabiliza a ENAP por contaminación en Quintero y ordena cierre de faenas", disponible en http://www.t13.cl/noticia/nacional/gobierno-responsabiliza-enap-contaminacion-quintero-y-ordena-cierre-faenas.

[8] La Tercera "Ministra Schmidt ordena paralizar algunas de las faenas de Enap en Quintero por emisión de gases tóxicos", disponible en https://www.latercera.com/nacional/noticia/ministra-schmidt-ordena-paralizar-todas-las-faenas-enap-quintero-podrian-estar-emitiendo-gases-toxicos/294058/

[9] Reporte de incidente por material peligroso, publicado por ONEMI el 4 de septiembre de 2018 a las 18:04 horas.

[10] Texto íntegro disponible en https://www.indh.cl/declaracion-de-consejo-indh-por-evento-de-contaminacion-en-quintero/

Durante el año 2011, el INDH realizó una Misión de Observación a la localidad de La Greda, Comuna de Puchuncaví, experiencia que se incorporó en el Informe Anual sobre la situación de los Derechos Humanos de ese año. En particular, se señaló que esta zona "configura una situación de injusticia ambiental evidente, por cuanto los beneficios que genera se reparten difusamente entre la sociedad toda, mientras que los costos ambientales son soportados por personas en situación de vulneración social y económica (p. 170)".

El 2014, el INDH nuevamente dedicó un capítulo de su Informe Anual a la zona conocida como cordón industrial de la Bahía de Quintero, reiterando que se podía "constatar una contaminación sistemática que incide en la vulneración de diversos derechos fundamentales" (p. 260) y señalando que "uno de los factores que agudiza la situación de la zona es que los instrumentos actuales sobre ordenamiento territorial y la Evaluación Ambiental Estratégica no permiten considerar la concentración de proyectos empresariales en los territorios, ni ver sus consecuencias acumulativas" (p. 254). A propósito de estas materias, el pasado 7 de septiembre, el Premio Nacional de Geografía, Doctor Hugo Romero Aravena, señaló:

> Envenenar el medio ambiente de lugares que constituyen el hábitat residencial de nuestros compatriotas es una muestra ineludible de injusticia ambiental y territorial y de una prepotencia insoportable. La injusticia ambiental está dada en primer lugar por la concentración desproporcionada de las fuentes contaminantes en ciertos lugares, hasta dañar en forma severa la salud de los habitantes y los ecosistemas y afectar, sin explicación alguna, la calidad de vida que está garantizada por la propia Constitución de la República y por los Derechos Humanos.[11]

Concordante con esta situación de injusticia advertida, los resultados del CENSO 2017, CASEN 2015 y otros datos públicos[12], evidencian la inequidad social y territorial que viven las comunas de Quintero y Puchuncaví:

- De las 1.815.902 personas que habitan la Región de Valparaíso, 31.923 residen en la comuna de Quintero y 18.546 en la comuna Puchuncaví, totalizando 50.379 habitantes en la zona afectada.

[11] Para mayor información, ver: http://www.uchile.cl/noticias/146920/en-una-geografia-justa-no-tienen-cabida-los-territorios-de-sacrificio.

[12] Reportes comunales de Puchuncaví y Quintero, elaborados por el Observatorio Social del Ministerio de Desarrollo Social, publicados el 17 de febrero de 2014; así como las estadísticas del Sistema Integrado de Información Social con Desagregación Territorial (SIIS-T), disponible en http://siist.ministeriodesarrollosocial.gob.cl/

- El promedio del acceso al agua potable entre ambas comunas es del 69,6%, versus el 94% que presenta la Región de Valparaíso. Dicha cobertura se desglosa de la siguiente manera:
    - 11.475 personas acceden al agua desde la red pública;
    - 3.934 personas lo hacen desde pozo o noria;
    - 1.044 tienen como fuente de abastecimiento camiones aljibe;
    - 130 personas consumen agua que proviene de río, vertiente, estero, canal, lago u otra fuente natural.
- En términos laborales, el 86% de la población de la zona declara trabajar en el sector servicios, mientras que solo el 6,6% lo hace en el sector industrial.
- El porcentaje de pobreza por ingresos a nivel nacional es del 11,7% y en la Región de Valparaíso alcanza el 12%. En la comuna de Quintero, este indicador se eleva al 15,8%, mientras que en Puchuncaví llega al 15%.
- En cuanto a los índices de pobreza multidimensional, se replica la situación anterior para estas dos comunas: 20,9% a nivel nacional y 18% a nivel regional, valores que aumentan al 26,7% en el caso de la comuna de Quintero y al 23,4% en Puchuncaví.
- Respecto de las evaluaciones SIMCE y PSU, los puntajes de los y las estudiantes de estas comunas están por debajo de la media regional y nacional.
- En el ámbito de la salud, la tasa de mortalidad infantil en Puchuncaví es superior a la media regional y se duplica la relativa a desnutrición o riesgo de desnutrición. Además, la esperanza de vida de las mujeres está por debajo de la media regional.

Estos y otros indicadores socioeconómicos indican que se combina una población que sufre importantes vulneraciones de derechos sociales con la existencia de una zona altamente contaminada, con escasa supervisión, control y sanciones a las fuentes contaminantes existentes. En el mismo sentido, el Mapa de Conflictos Socioambientales del INDH, recientemente actualizado, viene señalando -desde el año 2012 a la fecha- que la zona de la Bahía de Quintero presenta diversas disputas de esta índole y, a propósito del Informe Anual 2014, constituye una “Zona de Sacrificio”.

En la bahía de Quintero se localiza el cordón empresarial denominado Parque Industrial, que abarca las comunas de Quintero y Puchuncaví. Este fue “inaugurado en febrero de 1961, como un polo de desarrollo económico importante y una fuente significativa de trabajo para el sector”.[13] Actualmente, existen más de 17 empresas que desarrollan actividades económicas relacionadas con industrias para la fundición de cobre, elaboración

[13] Universidad Diego Portales. Informe Anual sobre Derechos Humanos 2012. Capítulo 5 “Empresas, medio ambiente y derechos humanos: la zona industrial Quintero-Puchuncaví”. Dominique Hervé, Judith Schönsteiner, Sylvana Mariangel e Ignacia Mewes. Ediciones UDP. Santiago de Chile. 2012, página 136.

de hormigón, asfalto y ladrillos; refinerías de petróleo e industrias químicas; generación de energía (instalación y operación de centrales térmicas); actividades portuarias, etc. Entre las empresas que allí operan, y que han generado importantes externalidades negativas para las personas que habitan el sector, se encuentran:

- La División Ventanas de CODELCO, dedicada a la refinería y fundición de cobre, oro y plata;
- El Complejo Termoeléctrico Ventanas y la Central Termoeléctrica Campiche, de propiedad de Aes Gener S.A.;
- La Planta de Lubricantes COPEC Loncura;
- El Terminal de Gas Natural Licuado (GNL Quintero);
- El Terminal Quintero de ENAP, que almacena petróleo crudo;
- Las Divisiones de Carbón y de Vapor de Comercial CATAMUTÚN;
- El Puerto Ventanas S.A., usado a la carga y descarga de concentrado de cobre;
- Cemento MELÓN, con instalaciones para el almacenamiento de materiales para la elaboración de cemento);
- OXIQUIM S.A., con su terminal marítimo de graneles líquidos;
- CORDEX, actual PACSA, que posee un terminal de combustible y asfalto;
- GASMAR S.A, con una central de abastecimiento de gas licuado;
- La Central Termoeléctrica NUEVA VENTANAS.

En cuanto a la situación normativa e institucional actual de la zona, las comunas de Concón, Quintero y Puchuncaví, hasta el año 2015, contaban con 8 estaciones de monitoreo de material particulado respirable (MP10) con representatividad poblacional (EMRP), ubicadas en Quintero, La Greda, Puchuncaví, Los Maitenes, Valle Alegre, Concón, Colmo y Junta de Vecinos. Mediante estas estaciones de monitoreo, y conforme a la Ley 19.300 sobre Bases Generales del Medio Ambiente, las autoridades competentes en salud y medio ambiente, declararon la zona como latente y saturada, para distintos componentes, según se indica a continuación:

1. Zona Latente por MP10. Con fecha 09 de junio de 2015, a través del Decreto N°10, se declaró como Zona Latente por Material Particulado Respirable (MP10). Lo anterior, basado la Norma Primaria de Calidad Ambiental para MP10, actualmente vigente, contenida en el DS N°20 de 2012, del Ministerio del Medio Ambiente. Esta establece los estándares de calidad para el contaminante mencionado en 150 microgramos por metro cúbico (150 microg/m3) y en 50 microgramos por metro cúbico (50 microg/m3), como concentración de 24 horas y anual, respectivamente.

2. Zona Saturada por MP 2,5. Con fecha 09 de junio de 2015, en virtud del mismo Decreto N°10, se declaró como Zona Latente por Material Particulado Fino Respirable (MP2,5),

elemento regulado actualmente en la Norma Primaria de Calidad Ambiental para MP 2,5 contenida en el DS N°12 de 2011, del Ministerio del Medio Ambiente. Esta establece los estándares de calidad para el contaminante mencionado en 50 microgramos por metro cúbico (50 microg/m3) y en 20 microgramos por metro cúbico (20 microg/m3), como concentración de 24 horas y anual, respectivamente.

Sobre estas dos declaraciones, es importante destacar que, conforme al artículo 43 inciso primero de la referida Ley 19.300, se establece que dicha determinación, sea por saturación o latencia, se hará mediante Decreto Supremo que llevará la firma del Ministro del Medio Ambiente y contendrá la determinación precisa del área geográfica que abarca. Además, incluirá la firma del Ministro de Salud si se trata de la aplicación de normas primarias de calidad ambiental.

3. Plan de Descontaminación vigente y proyecto de PDA presentado a la Contraloría General de la República. Conforme a lo dispuesto en el artículo 44 de la Ley 19.300, las declaraciones de zona saturada y zona latente referidas en los puntos anteriores, son condición necesaria para la elaboración de un Plan de Descontaminación o Plan de Prevención, respectivamente. Estos instrumentos de gestión ambiental tienen por finalidad recuperar los niveles señalados en las normas de calidad ambiental en una zona saturada, en el primer caso; y evitar la superación de una o más normas de calidad ambiental en una zona latente, en el segundo.

Con fecha 20 de diciembre de 2016, el Consejo de Ministros para la Sustentabilidad, presidido por el Ministro del Medio Ambiente de la época, presentó un Plan de Descontaminación para la zona. Sin embargo, el 26 de diciembre de 2017 este fue objetado por la Contraloría General de la República, a través del Dictamen N°44.528, argumentando que “no se ajusta[ba] a derecho”. En la actualidad, se encuentra vigente el PDA del Complejo Industrial Las Ventanas propuesto, conjuntamente por la Empresa Nacional de Minería, Fundición y Refinería Las Ventanas y La Planta Termoeléctrica de Chilgener S.A., que data del año 1992 y está concebido para abordar los niveles de anhídrido sulfuroso y material particulado respirable.

4. Programa de Recuperación Ambiental y Social (PRAS) de Quintero y Puchuncaví. Como consecuencia de la reconocida contaminación histórica existente en la zona, y ante la desprotección en la que se encuentran hace años las comunidades de Quintero y Puchuncaví producto de la actividad industrial que allí se desarrolla, se creó un Plan de Recuperación para Territorios Ambientalmente Vulnerables. De acuerdo a lo indicado por la propia autoridad medioambiental, el PRAS de Quintero y Puchuncaví es:

> Un programa multisectorial liderado por el Ministerio del Medio Ambiente, el cual busca el diálogo entre actores diversos que permita a los ciudadanos del territorio, mediante un modelo participativo, vivir en un ambiente libre de contaminación, así como también, señalar las prioridades de recuperación ambiental y social definiendo la gradualidad de su implementación.[14]

Este PRAS identifica 25 objetivos objetivos territoriales, el primero de ellos destinado precisamente a "disminuir los malos olores". Sin embargo, en razón de los úiltimos episodios críticos ocurridos en la zona, es posible señalar que el propósito trazado no se habría alcanzado. Sin perjuicio que la generación de este instrumento resulta positivo, en tanto reconoce los impactos ambientales en la zona, desde el punto de vista del trabajo multisectorial y con la sociedad civil, no es un instrumento de carácter normativo que permita su exigibilidad, no establece la autoridad a cargo de su fiscalización ni las sanciones respectivas ante un eventual incumplimiento. Por ende, si bien representa un avance, aún resulta insuficiente.

5. Norma de Emisión para Centrales Termoeléctricas. El ordenamiento jurídico vigente obliga al Estado a dictar normas de emisión que regulen las fuentes de contaminación, con el propósito de prevenir riesgos para la salud de las personas, resguardar su calidad de vida y el medio ambiente. En virtud de dicha obligación, con fecha 23 de junio de 2011, el Ministerio del Medio Ambiente publicó el Decreto 13/2011, norma específica que busca prevenir y controlar las emisiones atmosféricas generadas por centrales termoeléctricas, como las que operan en la aludida comuna de Quintero.

6. Norma de Emisión para Fundiciones. A propósito de las mismas obligaciones del punto anterior, el Ministerio del Medio Ambiente publicó, con fecha 12 de diciembre de 2013, el Decreto 28/2013 que establece normas de emisión para las fundiciones de cobre y otras fuentes emisoras de arsénico.

Así, y no obstante la actual existencia de al menos seis instrumentos normativos y de política pública, emitidos por distintas entidades estatales en diversas épocas, que tienen por objetivo proteger la vida y la salud de las personas, así como el medio ambiente, estos esfuerzos han sido insuficientes para prevenir la crisis ambiental de larga data que enfrenta la zona.

Para el INDH, desde su puesta en marcha el año 2010, la situación de la llamada "Zona de Sacrificio" localizada en las comunas de Quintero y Puchuncaví, ha sido de permanente

[14] Información proporcionada por el propio Ministerio de Medio Ambiente, disponible en https://pras.mma.gob.cl/quinteropuchuncavi/

preocupación, trayectoria que le habilita para consignar que las condiciones de vida que experimentan sus habitantes son de gravedad. En virtud de esto, es absolutamente necesario que las autoridades de Estado consideren las demandas manifestadas por la población afectada y las recomendaciones emitidas por diversas instituciones, adopten medidas urgentes, de corto, mediano y largo plazo, que permitan resguardar y garantizar los derechos humanos de sus habitantes.

Atendidos los antecedentes previamente expuestos, así como la grave situación experimentada por quienes habitan en ambas comunas producto del deterioro continuo de la calidad medioambiental, y que afecta diversos ámbitos de sus derechos humanos, el Consejo Directivo del INDH -en su sesión ordinaria N°442 del 27 de agosto del presente año- acordó la realización de una Misión de Observación a la zona de Quintero y Puchuncaví, cuyos resultados se exponen a continuación.

III. Objetivos de la Misión y Metodología de Trabajo

Objetivo general

Conocer los efectos que la crisis ambiental -de la Zona de Quintero y Puchuncaví- ha tenido en el ejercicio de derechos de sus habitantes, con especial foco en los derechos a vivir en un medio ambiente libre de contaminación, educación, salud, trabajo y vida digna.

Objetivos específicos

1. Establecer las afectaciones al derecho de vivir un medio ambiente libre de contaminación[15], derivadas de la crisis ambiental, que perciben las autoridades locales y habitantes de la zona.
2. Establecer en qué dimensiones ha sido vulnerado el derecho a la educación[16] de los niños, niñas y adolescentes de la zona, especialmente durante los últimos episodios ambientales críticos ocurridos en los meses de agosto y septiembre del presente año.
3. Conocer las principales afectaciones al derecho a la salud[17] experimentadas por quienes habitan la zona, con especial atención en la capacidad de respuesta de los Servicios de Salud en los períodos críticos.
4. Identificar en qué medida se ha afectado el derecho a la vida y a la integridad física y psíquica de los habitantes de la Zona de Quintero y Puchuncaví.[18]

[15] Artículo 19 N°8 de la Constitución Política de la República (CPR).
[16] Artículo 19 N°10 de la CPR; artículo 13.1 del Pacto Internacional de Derechos Económicos, Sociales y Culturales (PIDESC).
[17] Artículo 19 N° 9 de la CPR; artículo 12.1 del PIDESC.
[18] Artículo 19 N° 1 de la CPR.

5. Esclarecer cómo se afecta, producto de la crisis ambiental, el derecho al trabajo de quienes viven en la zona afectada por la crisis ambiental, y cómo aquello repercute en la posibilidad de detentar un nivel de vida digna.[19]

Metodología de la misión

Metodológicamente se optó por realizar un set de entrevistas semi estructuradas, especialmente diseñadas para la Misión de Observación, aplicadas a actores relevantes de la zona de Quintero y Puchuncaví -varios identificados de antemano y otros seleccionados bajo el método bola de nieve-, en virtud de los cuales fuera posible obtener una visión plural, que reflejara la heterogeneidad de puntos de vista, se relacionaran con distintas actividades económicas y de la vida local; a la vez que permitieran recabar evidencias y recibir denuncias concretas para efectos de colaborar en la construcción del Recurso de Protección que presentaría el INDH, una vez finalizada la Misión de Observación, el viernes 14 de septiembre ante la Ilustrísima Corte de Apelaciones de Valparaíso.

Para estos efectos, durante los días 11, 12 y 13 de septiembre de 2018, el INDH desplegó un equipo de 17 funcionarios -profesionales, técnicos y administrativos-, encabezado por su directora Consuelo Contreras Largo. En total, se realizaron 41 entrevistas -entre autoridades locales, usuarios y funcionarios del área de la salud y educación, estudiantes secundarios, pequeños comerciantes, pescadores artesanales y trabajadores de las industrias- y 5 encuentros grupales con organizaciones de la sociedad civil, visitando las localidades de La Greda, Las Ventanas y Horcón. Cabe advertir que algunas autoridades a quienes se les solicitó entrevista, indicaron no tener disponibilidad en su agenda para recibir al INDH.

IV. Sobre la constatación de afectación de los derechos humanos en la zona

En un Estado de Derecho como el nuestro son los Tribunales de Justicia quienes resuelven de acuerdo a la normativa vigente y a la interpretación de ésta, si una determinada situación ocurrida bajo su jurisdicción, se constituye como vulneradora o no de uno o más derechos. Se entenderá, *a priori*, para efectos de posibilitar la exposición de las diversas situaciones levantadas durante el trabajo de campo llevado a cabo por el INDH en el marco de la Misión de Observación, que entenderemos para el caso, que podría existir afectación de un Derecho Humano, cuando con ocasión de una acción u omisión por parte del Estado, el ejercicio de los derechos establecidos en la legislación nacional, así como en los instrumentos internacionales de derechos humanos ratificados por el Estado y vigentes en el ordenamiento jurídico interno, se vea impedido y/o limitado.

[19] Artículo 6.1 y 7 letra b) del PIDESC.

Así, y de acuerdo a los objetivos específicos, se señala a continuación un breve acápite de cada uno de los derechos respecto de los cuales se propuso identificar su eventual afectación: Derecho a vivir en un medio ambiente libre de contaminación, Derecho a la vida e integridad física y psíquica, Derecho al acceso a la salud, Derecho a la educación y Derecho al trabajo. Sin embargo, llevando a cabo el trabajo de campo, fue posible advertir otras situaciones que podían constituir afectación a otros derechos humanos, como son el acceso a la información y a la manifestación pacífica, que se describen al final de este apartado, además de encontrar en los habitantes de las comunas visitadas y afectadas por la crisis, una sensación de desesperanza y falta de proyecto de vida, para sí y sus hijos.

En cuanto al derecho a vivir en un medio ambiente libre de contaminación

La Constitución Política de la República, asegura en su artículo 19 numeral 8° el derecho a vivir en un medio ambiente libre de contaminación, siendo deber del Estado velar para que este derecho no sea afectado, debiendo además tutelar la preservación de la naturaleza. Tiene además el Estado la facultad de poder establecer restricciones específicas al ejercicio de determinados derechos o libertades para proteger el medio ambiente, y en este sentido es importante tener en cuenta la Ley de Bases Generales del Medio Ambiente N° 19.300 de marzo de 1994, que ya ha sido objeto de reiteradas modificaciones.

De acuerdo al trabajo de campo efectuado en la llamada "Zona de Sacrificio", las y los habitantes de la comunidad señalaron que, desde hace tiempo, varios años según algunos, conviven constantemente con *malos olores* y *nubes negras* que provienen de las chimeneas de las empresas ubicadas en la zona del cordón industrial, principalmente de noche, cuestión que también fue advertida por miembros del equipo del INDH. Además, los pobladores del lugar señalan, que viven con permanente dolor de cabeza y náuseas, y que, durante los episodios críticos, en que los *malos olores* y *nubes negras* serían aún más evidentes, se ven impedidos de desarrollar sus actividades habituales con normalidad.

Los relatos de los pescadores artesanales de la zona, son bastantes contundentes en orden a atribuir a la actividad industrial en la zona la afectación al medio ambiente y las consecuencias que aquello tendría en la afectación de otros derechos, como el trabajo y vida digna. Los pescadores artesanales señalan que, desde hace un tiempo, previo a los episodios críticos de agosto y de septiembre de 2018, hay especies marinas, como la jibia, que ya no se ven en el mar; pero que además han visto RILES[20] y RISES[21] vertidos en la zona de la Bahía, y que las empresas de la zona pagarían a pescadores entre $20.000 y $25.000 diarios por recoger los residuos, por ejemplo de carbón que provienen de las industrias y

[20] Residuos Industriales Líquidos.
[21] Residuos Industriales Sólidos.

varan en las costas de la Bahía en horas de la madrugada y entregar dichos sacos a las empresas que los producen y vierten al mar, cuestión que ha sido advertida también por otros habitantes de la zona a través de publicaciones en redes sociales, fotografías y videos que fueron compartidos con integrantes del equipo del INDH.

En este sentido, lo advertido por las máximas autoridades municipales de la comuna de Quintero, quienes señalaron que están realizando las primeras acciones para crear una unidad de control medioambiental al interior de la Municipalidad, encargada principalmente del monitoreo sistemático de las condiciones de calidad del aire, es coherente con los relatos de las y los habitantes, que indican que los monitoreos en la zona no han sido permanentes en el tiempo ni los han efectuado las autoridades locales. Las autoridades de la zona asumen que no existen ni protocolos ni normas asociadas a la situación de emergencia, que no existe institucionalidad local que aborde los temas medioambientales, que no hay manuales de acción que puedan activarse en estos casos críticos, dejando por tanto a la improvisación de las autoridades la ejecución de acciones en situaciones de emergencias, y que además no existen dispositivos nacionales estandarizados para el abordaje de emergencias medioambientales, evidenciándose por tanto un vacío normativo que perjudica de manera directa a la zona y a sus habitantes.

La comunidad de la zona sostiene - cuestión que puede ser corroborada si se revisan los estudios, informes y reportajes de prensa desde hace varios años atrás - que esta situación de afectación del medio ambiente es crónica, con ciertos episodios críticos que han sido mediatizados fuertemente, pero que sin embargo evidencia que estamos ante una situación que se ha mantenido acumulativamente en el tiempo y que por tanto la afectación al derecho a vivir en un medio ambiente libre de contaminación estaría siendo vulnerado no recientemente, si no desde hace años en la Zona. Esto implica que el Estado de Chile no ha resguardado ni garantizado el derecho que la propia Constitución de la República le reconoce a lo habitantes del país y con ello a los de las comunas de Quintero y Puchuncaví. En plena concordancia con lo descrito, y desde la vereda de quienes se desempeñan en cargos de autoridad en las empresas estatales, las declaraciones realizadas al equipo del INDH en el contexto de la Misión, por el Gerente General de la ENAP, son contundentes en orden a señalar que, si de verdad se aplicara el estándar internacional, Codelco, por ejemplo - que tiene una refinería para la pequeña minería en el parque industrial - tendría que pagar multa y ENAP seguiría operando sin problemas, ya que cuentan con sistemas de monitoreo en Concón (4) y en Quintero (2), sin embargo advierte que la realidad es que hay 15 empresas en el *parque industrial* y sus sistemas de monitoreos no son de fiar. Además, el entrevistado señala que es necesario hacer un estudio de base, ya que todas las empresas tienen impacto en el medio ambiente. Enfatiza el Gerente General de la ENAP, que la zona de la Bahía de Quintero no tiene línea de base, lo que advierte, es un requisito clave para

medir el impacto, siendo además del todo viable que las empresas adopten la decisión de apagar las fábricas para poder tomar las primeras mediciones y de ahí en más, ir tomando nuevas evaluaciones en el tiempo, no advirtiendo ningún obstáculo *per se* al menos en aquello, ya que nos comenta que todo el *parque* industrial lo hace permanentemente cuando se debe hacer mantención a las maquinarias industriales. Agrega, que a su juicio las soluciones estatales han sido pobres; básicamente, por el costo económico que implica cerrar las fábricas y que las medidas serias a mediano y largo plazo debiesen ser, junto al establecimiento de las líneas de base, el auditar las medidas de emergencias de todas las empresas del *parque*, instalar un observatorio ambiental, que incluya a todos los actores, y robustecer los métodos de fiscalización.

En cuanto al derecho a la vida y salud

La Constitución Política de la República, asegura en su artículo 19 numeral 1° el derecho a la vida y a la integridad física y psíquica; en su numeral 9° el derecho a la protección de la salud, debiendo garantizar el libre e igualitario acceso a las acciones de promoción, protección y recuperación de la salud y de rehabilitación del individuo que lo requiera, correspondiéndole asimismo, la coordinación y control de las acciones que se relacionen con la salud, siendo un deber preferente del Estado garantizar la ejecución de las acciones de salud, ya fuese a través de instituciones públicas o privadas. A su vez, el artículo 12.1 del PIDESC, obliga al Estado de Chile a reconocer el derecho de toda persona al disfrute del más alto nivel posible de salud física y mental. En el numeral 2 del mismo artículo, letra b) señala que de entre las medidas que deberá adoptar el Estado parte del Pacto, figura el mejoramiento en todos sus aspectos de la higiene del trabajo y del medio ambiente.

Quienes accedieron a contestar las entrevistas efectuadas por el equipo del INDH, nos relataron en primera persona las afectaciones que han sufrido y sufren actualmente a su salud. Señalan, atendido el tiempo que llevan habitando el lugar y las consecuencias de aquello, que existiría un nexo causal entre las precarias condiciones de su estado de salud en las que se encuentran ellos o sus familiares directos y la actividad industrial de las empresas emplazadas en la zona de la Bahía. Nexo causal que se condice con lo declarado por el Presidente de la República, Sr., Sebastián Piñera Echeñique, el pasado 28 de agosto de 2018 a la prensa nacional:

> […] sabemos que hay un grave problema con el agua en estas comunas. Mucha gente se nutr[e] de agua de pozos que están contaminados, algunos con arsénico, y eso envenena; […] estamos seguros que existe una relación entre la mala calidad del agua y los altos índices de cáncer que afectan a los habitantes de estas comunas.[22]

[22] Para mayor información, revisar en Ahora Noticias 28/08/18 (http://www.ahoranoticias.cl/noticias/nacional/234530-pinera-en-quintero-mucha-gente-se-nutre-de-agua-de-pozos-que-estan-contaminados.html)

Los últimos episodios críticos en la zona, habrían implicado tal nivel de gravedad en la afectación de la salud de sus habitantes, que, como es de público conocimiento, más de 300 personas debieron ser atendidas de urgencia en centros asistenciales de salud por síntomas de intoxicación según indicaron las autoridades y la prensa nacional.

En tal sentido, los testimonios obtenidos en la Misión de Observación fueron esclarecedores:

> El día de la crisis había incredulidad y enojo. Se había estado en charla 3 años atrás y en esa época el Colegio Médico predijo lo que ocurriría pues la situación era grave. Hubo estudios que se hicieron y que no dan confianza sobre resultados. Luego, [haciendo referencia a los días posteriores a los episodios de crisis] se empezaron a ver niños con piernas "muertas", con alergias. Fui testigo de una mujer que tuvo un aborto del 21 al 22 de agosto.

Una voluntaria de la Casa de la Mujer y miembro de "Mujeres en Zona de Sacrificio" señaló:

> El 23 de agosto hubo un olor asqueroso en el pueblo y el 24 nuevas sirenas e información de intoxicados con sus fotos en las redes. El alcalde estaba en terreno y se le pidió ser firme para exigir el fin a la contaminación. Se constituyó mesa de trabajo esa semana y llegaron autoridades: seremis, intendente formándose Comité Operativo de Emergencia (COE), luego se sumaron los políticos de RN, todo a puertas cerradas. No sabían qué hacer pues no hay planes para esta situación. A esa altura habían 64 NNA intoxicados. Le echaron la culpa a la ENAP. Luego llegó una "maquinita" para medir contaminación. Capacitaron a la jefa de oficina ambiental del municipio [Quintero]. La usaron y decretaron "alerta amarilla" sin que se supiese las implicancias concretas, para luego suspender clases. No creemos en la maquinita.

Esto último encuentra su correlato en lo señalado por un funcionario del Ministerio del Medio Ambiente, de Santiago, quien se encontraba midiendo la calidad del aire en uno de los Liceos en toma en la localidad de Las Ventanas, visitados por el equipo del INDH, quien amablemente explicó cómo funcionaba la máquina de escáner dispuesta por el Gobierno para la Bahía de Quintero y Puchuncaví, advirtiendo que como la máquina se adquiere por parte del Ministerio, ya programada con los 120 gases que pudiese identificar, no es 100% fiable, primero porque de no estar en la memoria de la máquina el gas que circula en el aire, no será captado ni medido y por tanto no se sabrá finalmente todos los tipos de gases que circulan en el aire, y segundo, porque la medición, al no ser permanente ni continua, no es contundente en cuanto a la cantidad en la que se encuentra determinado gas en determinado periodo de tiempo. Didácticamente, señaló que la máquina de escáner

"*tomaba una foto*" y lo confiable sería "*que grabe un video*" de lo que ocurre en la zona, durante las 24 horas de días, dispuesta además en distintos sectores de la bahía.

La gravedad de esta situación, descrita por los habitantes de las comunas afectadas, se ve formalmente confirmada por la "alerta amarilla" decretada por las autoridades, atendida la emergencia ambiental decretada en la Zona, denominación que, según lo informa la propia Oficina Nacional de Emergencia (ONEMI) del Ministerio del Interior y Seguridad Pública, se establece cuando una amenaza crece en extensión y severidad, lo que lleva a suponer que no podrá ser controlada con los recursos locales habituales, debiendo alistarse los recursos necesarios para intervenir, de acuerdo a la evolución del evento destructivo. Sin embargo, a pesar de esta situación de riesgo la población señaló insistentemente no conocer Planes de Acción ante las emergencias; cuestión similar ocurre en las algunas empresas de la Zona.

En cuanto al derecho a la educación

La Constitución Política de la República, asegura en su artículo 19 numeral 10° el derecho a la educación, señalando que la educación tendrá por objeto el pleno desarrollo de la persona en las distintas etapas de su vida. A su vez, el artículo 13.1 del PIDESC, obliga al Estado de Chile a reconocer el derecho de toda persona a la educación, debiendo orientarse hacia el pleno desarrollo de la personalidad humana y del sentido de su dignidad, debiendo fortalecer el respeto por los derechos humanos y las libertades humanas.

La realidad que viven actualmente las comunas de Quintero y Puchuncaví dista de la efectiva garantía estatal en cuanto al ejercicio del derecho a la educación. En este sentido, a la fecha de la Misión de Observación 9 establecimientos educacionales de la comuna de Quintero y 14 de la comuna de Puchuncaví, habían visto alterada la programación del año escolar y no podrían someterse finalmente al sistema de evaluación general. Resultaron bastante gráficos los testimonios otorgados por los estudiantes de la Zona, cuyos colegios y liceos estaban "En Toma Pacífica", atendido que las clases estaban suspendidas previamente por disponerlo así las autoridades, en atención a la "alerta amarilla" decretada en la zona.

Si bien la mayoría de las y los entrevistados reportaron que continuaban recibiendo las becas de alimentación JUNAEB, la sensación de que las autoridades comunales y de Gobierno les han mentido, les han faltado el respeto y han optado por suspender las clases y cerrar los establecimientos educacionales, en vez de suspender al menos provisoriamente la actividad industrial que identifican como la causa de la crisis ambiental, es una cuestión generalizada en el estudiantado. Desde el patio de uno de los establecimientos a los que ingresó el equipo del INDH en la localidad de Las Ventanas, el Complejo Educacional Sargento Aldea, era visible a horas del mediodía del miércoles 12 de septiembre, observar

las nubes de humo color gris que emanaban desde las chimeneas de las empresas Ventana 1, Ventana 2, Nueva Ventana y Campiche.

Los testimonios del estudiantado, que encontraron su correlato en lo señalado por las autoridades, afirman que las medidas adoptadas por éstas, atendida la suspensión de las clases, ha sido disponer de una plataforma digital para las asignaturas básicas y reforzamiento de guías de estudio en algunos puntos de la Zona. Medidas que, según los estudiantes, no asegura la accesibilidad a ese material por parte de todos, ya que no se atiende a las condiciones de habitabilidad y acceso, además que serían materiales de "repaso" de materias.

Los estudiantes aseguran, además, que no se les ha informado de qué manera podrán cumplir con el curriculum nacional, si serán sometidos a la evaluación SIMCE y si los estudiantes que cursan 4° año de Enseñanza Media tendrán alguna consideración especial para rendir la PSU. Cabe advertir, que la mayoría de los estudiantes entrevistados advierten que han recibido apoyo permanente por parte de sus profesores, de manera informal, y que han mantenido la comunicación y contacto directos con éstos, no así con las autoridades de la Zona, ni tampoco con las empresas ubicadas en el cordón industrial de la bahía.

Lo descrito, permitiría afirmar que el Estado no ha garantizado el ejercicio del derecho a la educación consagrado a nivel constitucional en el ordenamiento jurídico nacional, verificándose que a raíz de los episodios de contaminación, los niños, niñas y adolescentes de las comunas de Quintero y Puchuncaví no han podido ejercer su derecho a la educación, en primer lugar, a raíz de los episodios de intoxicación que sufrieron en sus establecimientos educacionales y luego, cuando posterior a los episodios de intoxicación se decretó la alerta amarilla y se ordenó la suspensión de clases y actividades educativas en resguardo de su salud, pero sin una información y planes muy efectivos.

En cuanto al derecho al trabajo

La Constitución Política de la República, atendido el inciso 2° de su artículo 5° que señala que es deber de los órganos del Estado respetar y promover los derechos garantizados por los tratados internacionales ratificados por Chile y que se encuentren vigentes, asegura a través del artículo 6.1 del PIDESC, el derecho de toda persona a trabajar, derecho que comprende el tener la oportunidad de ganarse la vida mediante un trabajo libremente escogido o aceptado y del artículo 7° letras a) numeral ii) y b) del mismo Pacto Internacional suscrito y vigente, el derecho de toda persona al goce de condiciones de trabajo equitativas y satisfactorias que le aseguren en especial las condiciones de existencia dignas para ellos y para sus familias y la seguridad e higiene en el trabajo.

En relación a este derecho, se recogieron por parte del equipo del INDH los testimonios de pequeños comerciantes y pescadores artesanales, que refirieron de manera generalizada una baja en sus ingresos atendida la crisis ambiental que se vive en la zona y que repercute en distintas actividades comerciales que constituyen para ellos sus fuentes de trabajo y por ende de ingresos. El testimonio de una artesana de Horcón, advierte específicamente la situación descrita, señalando que hace unos 15 años comenzó a decaer el turismo, y que desde hace tres fines de semana que no ha vendido nada: "Yo le preguntaba a mi hija ¿será que no hay nadie por lo de la contaminación?". Señala además, que es preferible que en el mes de septiembre no pase nada, que no venga nadie, pero que "se corte el hilo, que tengamos responsables, que tengamos sanciones y que empecemos de nuevo", en relación a que todavía no se establece formalmente por las autoridades cuál o cuáles serían las causas de la crisis ambiental que vive la Zona, y nos plantea que su principal preocupación es que se desate una emergencia en época de verano y no lleguen más turistas al lugar.

En el mismo sentido, los testimonios de trabajadores industriales contratistas, quienes nos señalaron que han sufrido una baja en sus remuneraciones, por la reducción de los turnos, además de mantener una marcada incertidumbre laboral, y estar preocupados por su estado de salud al trabajar en las empresas ubicadas en el cordón industrial, aunque no viven en las comunas, están 10 horas trabajando en la zona afectada. Esta última declaración, advierte que las industrias emplazadas en la Zona de la Bahía de Quintero no necesariamente dan trabajo a los habitantes de las comunas de Quintero y Puchuncaví, lo que tiene su correlato con los datos del Censo 2017 y Casen 2015, en cuanto a que los habitantes de la zona no estarían empleados necesariamente en sector industrial, confirmándose así lo advertido por el Premio Nacional del Geografía, Doctor Hugo Romero Aravena, y señalando *infra,* en cuanto a que los habitantes de la zona soportan los costos de vivir en una zona industrial, más no las ganancias de aquella productividad. El testimonio de un pescador artesanal resulta ilustrador en ese sentido: "las empresas de acá no dan mucho empleo a los de acá. La actividad económica depende de la pesca y el turismo y las empresas los están corriendo".

Como se señaló al inicio de este subapartado, se constató además en terreno, un marcado grado de desinformación generalizada en los habitantes de la Zona, en cuanto a ciertas cuestiones relativas a la crisis ambiental, además de estar siendo la población según los reportes de las y los propios habitantes, reprimida y amedrentada a la hora de manifestar su preocupación por la situación que les toca vivir y su disconformidad con las decisiones de las autoridades, y constatar a través de sus relatos un descontento generalizado y una falta de proyecto de vida, atendida la desconfianza en las decisiones que otros tomarán por

ellos y la incertidumbre ante las consecuencias negativas que la crisis seguiría trayendo para la zona y sus habitantes.

La Constitución Política de la República consagra en su artículo 19 numeral 13°, el derecho a reunirse pacíficamente sin permiso previo y sin armas, el numeral 14° resguarda el derecho a presentar peticiones a la autoridad sobre cualquier asunto de interés público o privado y el numeral 15° el derecho de asociarse sin permiso previo. A propósito de las afectaciones a sus derechos, atendida la crisis ambiental que soportan hace décadas los habitantes de la de las comunas de Quintero y Puchuncaví, han organizado diversas manifestaciones públicas, participando el INDH en la observación de la mayoría de éstas, reportando su finalización sin problemas. Sin embargo, habitantes de las distintas localidades de la zona afectada, nos reportaron situaciones de represión policial hacía la población, específicamente en el sector de La Greda el pasado sábado 8 de septiembre en el momento de la manifestación. Y de manera generalizada, los entrevistados señalaron que los agentes policiales han comenzado a hacer un uso excesivo de la fuerza, que cada vez está siendo más común la presencia policía en las afueras de los colegios, liceos, casas particulares, particularmente de Fuerzas Especiales de Carabineros, cuestión que califican como absolutamente inédito para la Zona, pues nunca antes habían experimentado situaciones como las descritas, presencia que fue advertida también por el equipo desplegado en terreno del INDH durante la Misión. La declaración de un pescador artesanal en este sentido, resume lo señalado por varios entrevistados: “Estamos sitiados por fuerzas policiales. Ha habido represión excesiva. Amenazaron a un dirigente, al secretario de nuestro sindicato. Quieren frenar las movilizaciones metiendo miedo”.

En cuanto a las Leyes 20.285 y 20.417, y respecto al derecho de todas las personas a tener acceso a la información de manera oportuna y adecuada, y a participar de manera significativa en las decisiones que afectan sus vidas y su entorno, la realidad constatada a través de los testimonios recogidos durante la Misión de Observación señalan sistemáticamente el desconocimiento por parte de los habitantes de la Zona, de lo que significa “alerta amarilla”, las acciones que les corresponde tomar para protegerse, los elementos que tendrán a su alcance y las obligaciones que les corresponden a las autoridades. Incluso en el sector industrial se pudo constatar que una de las empresas no ha recibido información de las autoridades durante toda la situación crítica. Los habitantes se informan de manera informal, a través de rumores o publicaciones particulares en redes sociales; existe confusión entre los pobladores lo que deriva en sensación de angustia permanente advertida por muchos y dicha incertidumbre se debería en gran parte a la falta de información oportuna, veraz, fiable y comprensible que deben proveer las autoridades. Se pudo constatar que existen obstáculos normativos (solo algunos elementos regulados por el legislador) y fácticos (falta de equipamiento y equipos adecuados para conocer los

elementos contaminantes que están afectando a la población) con el fin de acceder a la información sobre los materiales y actividades peligrosas respecto de las comunidades de la Zona, y los efectos o consecuencias adversas para ellas, no obstante haber sido solicitadas a las autoridades correspondientes, asimismo no hay diagnósticos claros sobre los estados de salud de la población, los diagnósticos, sus tratamientos médicos - farmacológicos y su continuidad y gratuidad.

Lo descrito, deriva en una sensación generalizada en la población de desconfianza en las instituciones del Estado, en las autoridades comunales, regionales y nacionales, en las decisiones que dichas autoridades toman y que repercuten de manera directa en sus vidas y las de sus familiares. Los habitantes sostienen abiertamente que el Estado de Chile ha privilegiado la inversión, la industria, la producción empresarial y sus ganancias, y nos sus derechos. Lo descrito tuvo su correlato en los estudiantes, pescadores, trabajadores, habitantes que hoy padecen enfermedades de origen desconocido o cuyos familiares han fallecido, se presentaron ante el INDH como "soy nieto de uno de los hombres verdes". En este sentido, es necesario señalar que:

> La dignidad […] no es un concepto abstracto. Se relaciona con las condiciones reales de la existencia humana que posibilitan o niegan el ejercicio de las libertades y el desarrollo de la vida con bienestar. Un Estado en el que la dignidad humana […] no esté garantizada de manera adecuada, es responsable de dañar el proyecto vital de los ciudadanos. El concepto del daño al proyecto de vida es de un valor inestimable para entender de manera integral las violaciones a los derechos humanos y las perspectivas en que se deben reparar.[23]

V. Recomendaciones

En atención a lo descrito, y cumpliendo el INDH con su mandato legal, se recomienda al Estado de Chile, en el marco de su deber de protección de todos los habitantes del territorio nacional que:

1. Implemente a la brevedad, a través del Ministerio de Salud y Medio Ambiente, una **Campaña de Información** dirigida a la población de las comunas de Quintero y Puchuncaví, que implique informar de manera oportuna, veraz, confiable y comprensible a todos y cada uno de sus habitantes, acerca del actual estado de la crisis ambiental y sanitaria que afecta a la zona, indicando las causas y efectos de esta, las medidas oficiales que se toman y su evaluación, de manera de mitigar la desinformación que existe al respecto en la población.

[23] Herreño Hernández, Ángel. ¿Todo o nada? Principio de Integralidad y derechos sociales. Pág., 65. Editorial: Textos de aquí y ahora. Colombia, enero de 2008.

2. Promueva las mejores prácticas sobre acceso a la información, participación pública y acceso a la justicia en asuntos ambientales conforme a los tratados internacionales sobre derechos humanos, en línea con lo establecido con el Acuerdo Regional sobre el Acceso a la Información, la Participación Pública, y el Acceso a la Justicia en Asuntos Ambientales en América Latina y el Caribe, conocido como el Acuerdo de Escazú, esto con el objeto de resguardar el derecho de los habitantes del territorio nacional a acceder a la información relativa a asuntos ambientales que repercuten de manera directa sobre sus vidas así como la posibilidad de participar en las actividades que les afecten en la temática en cuestión.

3. Lleve a cabo a la brevedad, **las mediciones de contaminantes en aire, suelo y aguas** -de consumo humano, proveniente de los servicios de agua potable de la zona o de pozo, así como de las aguas marítimas que bordean la bahía de Quintero-, enmarcándolas en los más altos estándares internacionales prescritos por la Organización Mundial de la Salud; y asegurando que en dichos procedimientos de medición participen representantes de la sociedad civil, de modo de mitigar la desconfianza generalizada que actualmente existe en la zona.

4. Garantice a la brevedad a los habitantes de la zona, a través del Instituto de Salud Pública, la realización de manera **planificada y gratuita de los exámenes toxicológicos** necesarios que permitan determinar con **certeza e imparcialidad**, la existencia o no, de contaminantes en el cuerpo de los habitantes (sangre, orina o metabolitos), esto, con el fin de garantizar el acceso a los tratamientos farmacológicos que permitan detener el deterioro de su estado de salud física y psíquica, como asimismo establecer la asociación entre éstos y las fuentes contaminantes que permitan a posteriori, establecer las responsabilidades al respecto.

5. Ordene y habilite a los Servicios de Salud de la zona, **la implementación de un sistema de monitoreo permanente,** efectivo y veraz, respecto del estado de salud de los habitantes de la zona y su potencial afectación a largo plazo, con el fin de mantener un registro actualizado de los estados de salud de la población, que responda especializadamente con eficacia y de forma articulada ante la eventualidad de nuevas crisis sanitarias en el marco de problemas ambientales agudos.

6. Ordene y habilite a la Superintendencia del Medio Ambiente y a cualquier otra institución con competencia ambiental que resulte pertinente**, la implementación de sistemas de medición de las emisiones, que sea monitoreado de manera independiente, con autonomía técnica, permanente, efectiva y veraz -con participación de miembros que den confianza a la comunidad-, en lugares adecuados,** que provengan de las industrias estatales y particulares, actualmente operativas en el cordón industrial de la Bahía de

Quintero, que resultan sindicadas por los habitantes de la Zona, como los principales responsables de la actual crisis ambiental.

7. Elabore a la brevedad, el **Nuevo Plan de Descontaminación para las comunas de Quintero y Puchuncaví**, el cual debiese estar en concordancia con los más altos estándares establecidos por los organismos internacionales de salud y medioambientales especializados en la materia, con el objetivo de dejar sin efecto el Plan del año 1993 -actualmente vigente para la zona- y que ha evidenciado en estos años y los últimos episodios críticos no cumplir con los resguardos necesarios para la salud de quienes habitan las comunas de Quintero y Puchuncaví.

8. Presente, a través del MINEDUC, un plan de contingencia para la zona donde se aborden los plazos del calendario escolar, que brinde cobertura al curriculum nacional, considerando a todo el estudiantado en general y, en particular, a los niños, niñas y adolescentes del Programa de Integración Escolar. A su vez, se recomienda considerar medidas especiales para las y los estudiantes de cuarto medio que este año rendirán la PSU, con apoyo especializado. Asimismo, se debe consultar al profesorado que rendiría su evaluación en el Sistema de Desarrollo Profesional Docente, con el objeto de no perjudicar su carrera e ingresos.

9. Ingrese un proyecto de reforma de ley con suma urgencia respecto de la actual normativa sobre Bases Generales del Medio Ambiente, Ley 19.300, que -atendida la actual crisis ambiental que nos convoca- ha evidenciado no cumplir con los actuales estándares internacionales que garantizan el derechos de la población a vivir en un medio ambiente libre de contaminación. Esto implica una contradicción con la Constitución Política de la República, así como los Tratados Internacionales de Derechos Humanos ratificados por el Estado de Chile y vigentes actualmente en nuestro ordenamiento jurídico, que aseguran a todos los habitantes del territorio nacional a vivir en un medio ambiente libre de contaminación y obligan al Estado a resguardar la naturaleza. En este sentido, es sumamente necesario que la mencionada legislación establezca la tipificación de delitos ambientales, obligue a regular las emisiones de todo tipo de agentes contaminantes que pudiesen o no resultar nocivos a la población, adecuando dichas normativas a los estándares que establecen los organismos internacionales expertos en la materia, referentes a aguas dulces y saladas, aire y suelo; así como asegurar los mecanismos que permitan una participación efectiva y con incidencia por parte de la ciudadanía, lo que implicará para el Estado de Chile proceder con la debida diligencia que ameritan temáticas como estas, al mismo tiempo que otorga un marco de acción legal que resguarde los derechos humanos de quienes habitan la zona, a las empresas e industrias que actualmente allí operan.

10. Recuerde a las empresas públicas y privadas el deber de respeto de los derechos humanos de las comunidades en las cuales llevan a cabo sus actividades productivas. Es importante que las empresas localizadas en la zona asuman la necesidad de incorporar en sus políticas los Principios Rectores sobre las Empresas y Derechos Humanos de Naciones Unidas y los estándares que de ellos se derivan para su actuar, con especial énfasis en el principio operativo N°17 que hace referencia a que "las empresas deben proceder con la **debida diligencia** en materia de derechos humanos", con el fin de "identificar, prevenir, mitigar y responder de las consecuencias negativas de sus actividades sobre los derechos humanos". Esto requiere, además, que las empresas incorporen en sus procesos la gestión de riesgos y que "no se limiten a identificar y gestionar riesgos importantes para la propia empresa, sino que incluyan los riesgos para los titulares de derechos".[24]

11. Disponga que las **Fuerzas Especiales de Orden y Seguridad, tomen las máximas providencias y resguardos respecto del accionar policial**, con el objetivo de cautelar el derecho de los habitantes de la zona a manifestarse de manera pacífica, sin ser reprimidos ni amedrentados en el ejercicio legítimo de este.

12. Modifique, a la brevedad, **los actuales instrumentos que rigen el ordenamiento territorial de la zona, el Plan Regulador Metropolitano de Valparaíso** y se congelen las autorizaciones de inversión en las 754 hectáreas aún disponibles para actividades industriales peligrosas. Asimismo, considera necesaria la modificación del **actual Sistema de Evaluación Ambiental,** que no permite considerar la concentración de proyectos empresariales en los territorios ni ver sus impactos acumulativos, ambas cuestiones ya advertidas por el INDH en su Informe Anual del año 2014.

[24] En este sentido, el l INDH ha realizado a través de sus informes anuales sobre la situación de los derechos humanos en Chile de los años 2013, 2016 y 2017, recomendaciones al Estado y a las empresas, para que se revisen "las políticas y prácticas vigentes sobre la actividad empresarial y los derechos humanos según los Principios Rectores de Naciones Unidas sobre Empresas y Derechos Humanos (2013, pág. 271).

Observaciones Depto MA Colegio Médico de Chile
Anteproyecto Plan de Descontaminación y Prevención Atmosférica (PPDA) Concón, Quintero y Puchuncaví
Res. Ex. Nº 1030 de 30 de octubre de 2018 del Ministerio del Medio Ambiente

Contenido del formulario:

En la primera tabla "I. Observaciones Generales al anteproyecto de PPDA y sus antecedentes", se ofrece un espacio libre para formular observaciones generales al PPDA, a sus antecedentes técnicos y a su contexto, incluyendo los vacíos que éste proceso pueda tener.

En las tablas nº 2 a la nº 4, se ofrece un apartado para realizar observaciones a los antecedentes públicos que sirven de base al anteproyecto (los cuales constan en el expediente electrónico: http://planesynormas.mma.gob.cl/normas/expediente/index.php?tipo=busqueda&id_expediente=934394) De estos antecedentes, los principales son: (i) el Inventario de Emisiones; (ii) Informe de la SEREMI del Medio Ambiente; y (iii) el AGIES. Por motivos de espacio estos documentos no han sido transcritos en el formulario, sin perjuicio de lo cual pueden ser revisados y tenidos en cuenta para estas observaciones, por lo cual se otorga un espacio para ello, y en el caso del AGIES, este espacio considera los principales temas abordados en este.

Finalmente, en la tabla nº 5, se establece un apartado para realizar observaciones específicas al articulado del anteproyecto, por lo cual el contenido de este ha sido traspasado a la columna izquierda, dejando la columna de la derecha para poder manifestar observaciones particulares a cada materia o artículo.

1. Observaciones Generales al anteproyecto de PPDA y sus antecedentes
Nombre: Andrei N Tchernitchin (Andrés Tchernitchin Varlamov) Jerarquía/cargo: Presidente, Departamento de Medio Ambiente del Colegio Médico de Chile, Profesor Titular U de Chile, Postdoctoral Fellow Population Council University of North Carolina & University of Pennsylvania Depto M.A. Colegio Médico de Chile Observaciones: ***Análisis de los objetivos del plan de descontaminación de Q-P-C*** En **los antecedentes del plan se señala que a lo largo del tiempo las emisiones se han mantenido, ha habido estabilidad, e incluso muestran tendencia a la disminución**, entonces **¿por qué se produce la crisis sanitaria y ambiental de la zona?** Si el plan de descontaminación tiene el objetivo de volver a las normas que regulen solamente

los contaminantes que están reguilados (MP10, MP2,5 y SO_2), que no solo se han mantenido, sino que tienden a su disminución, y ocurren crisis sanitarias cada vez más graves, eso **puede indicarnos que el plan no sirve realmente y que los compuestos más peligrosos son otros**.

Tomando en cuenta lo anterior, y considerando que en la zona de Quintero Puchuncaví y Concón existen numerosas industrias en las cuales varios procesos son causantes de emisión de diversos contaminantes dañinos para la salud humana, se deduce claramente que el plan de descontaminación debe normar todos los agentes químicos que son emitidos por el Complejo Industrial, y no solo por las chimeneas, sino que, muchas veces en forma predominante, como emisiones fugitivas y/o descargas de compuestos de otra manera, por ejemplo, en cuerpos de agua. Por lo tanto, lo que se debe alcanzar son las normas primarias (que tienen relación con la salud humana) y secundarias, de todos los agentes contaminantes, y no solo aquellos que son considerados actualmente en entre las normas de nuestro país, es decir, deben incluir también aquellos que son recomendados por la OMS y/o son considerados en las normas de otros países.

Situación actual

En la zona de Quintero Puchuncaví y Concón existen numerosas industrias en las cuales varios procesos son causantes de emisión de diversos contaminantes dañinos para la salud humana. Entre los contaminantes principales se identifican los siguientes:

1. Metaloides y metales pesados
    a. Arsénico
    b. Plomo
    c. Cobre
    d. Cadmio
    e. Manganeso
    f. Vanadio
    g. Níquel

2. Gases inorgánicos
    a. Dióxido de azufre
    b. Vapores de ácido sulfúrico, neblina y lluvia ácida

c. Monóxido de carbono
d. Dióxido de nitrógeno
e. Ozono

3. Moléculas orgánicas (sólidas, líquidas, gaseosas o incorporadas a material particulado)
    a. Metano
    b. Hidrocarburos de cadena lineal no metánicos y sus isómeros
    c. Hidrocarburos cíclicos saturados e insaturados (ciclohexano, tolueno, xileno, benceno naftaleno, benzopireno y otros)
    d. Hidrocarburos clorados y con otros elementos formando parte de ellos (nitrobenceno,
    e. Moléculas orgánicas especialmente nocivas para la salud: dioxinas, furanos, policlorobifenilos (PCB), compuestos policíclicos aromáticos,
    f. Moléculas prohibidas por convenios internacionales firmados por Chile (tricloroetano “metil-cloroformo”)

4. Material particulado (MPS, MP10, MP2,5, MP ultrafino, además de polvo de tamaño de partículas mayor a MPS)

La exposición a los compuestos más arriba enumerados determina efectos adversos en salud, que dependen de la concentración de ellos (que en este momento para la mayoría de éstos no se cuantifica y muchas veces ni siquiera se identifica), del tiempo de exposición, de la etapa del desarrollo del sujeto expuesto (incluida las etapas embrionaria y fetal), de susceptibilidades especiales (enfermedades concomitantes, condición genética, etc.) y otras condiciones (exposición previa durante el periodo prenatal o infantil temprano a SO_2, dioxinas u otros compuestos, etc.).

1. La exposición a agentes tóxicos ambientales puede ser:
a. Aguda durante edad juvenil o adulta
b. Crónica durante edad juvenil o adulta
c. Prenatal precoz (embrionaria o inicio del período fetal)
d. Prenatal tardía (últimos 3 a 4 meses de gestación)
e. Infantil temprana (primeros años de vida postnatal)
f. Paterna o materna

2. Los principales efectos de dicha exposición pueden ser:

a. Efectos inmediatos o tempranos
b. Efectos progresivos reversibles
c. Efectos progresivos irreversibles
d. Efectos diferidos (en el tiempo)
    i. Mutaciones
    ii. Cáncer
    iii. Malformaciones fetales
    iv. Imprinting epigenético o desprogramación celular
    v. Otros (mecanismos indeterminados o poco conocidos)

La **exposición aguda** se refiere a minutos, horas, o hasta un par de semanas de duración. La **exposición crónica** se refiere a mayor tiempo que el de la aguda, meses o años, que puede ser continua, o ser constituida por numerosas exposiciones agudas durante un tiempo prolongado. Las **exposiciones prenatal, perinatal o infantil temprana**, que pueden ser agudas o prolongadas, se describen en forma separada por cuanto sus efectos en salud que son diferentes, el daño a la salud ocurre con dosis mucho menores. La exposición prenatal o perinatal puede ser indirecta, a través de la madre expuesta a algún agente ambiental tóxico, el que pasa al feto a través de la placenta, al recién nacido a través de la leche materna; la exposición infantil puede ser principalmente por vía inhalatoria, digestiva y con menos frecuencia transcutánea. Lo mismo sucede con la **exposición embrionaria o inicio del período fetal**, cuyos efectos también son muy diferentes de los anteriores.

Los efectos causados por exposición a algún agente ambiental pueden ser tempranos si ocurren con dosis muy elevadas de éste y ocurren horas o pocos días después de la exposición. Exposiciones a dosis menores en forma crónica o numerosas exposiciones agudas repetitivas causan efectos progresivos o acumulativos (algunos agentes se acumulan, otros no, los efectos adversos en sí pueden ser acumulativos). Los efectos clínicos pueden aparecer después de numerosas exposiciones agudas. Algunos efectos pueden producirse en forma diferida en el tiempo, a veces muchos años después de la exposición al agente, o aún, se manifiestan en las próximas generaciones.

Malformaciones fetales

- Son visibles o clínicamente detectables, y se producen por efecto de la exposición a estos compuestos durante los primeros meses de vida intrauterina. La exposición a diversos contaminantes ambientales incrementa la incidencia de malformaciones congénitas (Restrepo et al., 1990).

Mutaciones

- Son modificaciones, en algunas células del organismo, del material genético por efecto de la exposición a agentes físicos o químicos mutagénicos. Si ocurren el células somáticas, afectan a las células hijas, y desaparecen con la muerte del portador de estas células por lo cual no son hereditarias. El único riesgo que puede ocurrir es que ocurra una mutación que favorezca la transformación de una de esas células en célula cancerosa, la que sí provoca una enfermedad grave y frecuentemente mortal en el individuo portador. Si las mutaciones que ocurren en células de la línea germinal (células precursoras de los espermatozoides o de los oocitos), afectan el material genético heredable; su gravedad para la especie humana es la persistencia, a través de las generaciones, de patologías hereditarias generadas por este mecanismo, que sólo son eliminadas por selección natural cuando la mutación causa una dificultad a la sobrevivencia o reproducción del portador. Varios contaminantes ambientales suelen producir alteraciones cromosómicas, es decir, mutaciones.

Cáncer.

- La exposición a compuestos denominados carcinógenos promueve el desarrollo de tumores en sólo algunos órganos en forma específica, los que son diferentes para cada agente causal. Las diferentes incidencias de diversos cánceres en diferentes regiones o países se deben, al menos en parte, a la presencia de carcinógenos ambientales locales (Rivara & Corey, 1995).

- Es importante mencionar que cada agente carcinógeno sólo determina el desarrollo de cáncer en órganos específicos para ese agente, y no en cualquier órgano, y que para aquellos cánceres que son inducidos por muchos carcinógenos diferentes (pulmón, por ejemplo), existen cánceres que son típicos del agente causal. Así por ejemplo, el arsénico determina el desarrollo de cáncer broncopulmonar, de la vejiga y del riñón. El asbesto al contrario determina el desarrollo cáncer del pulmón y del mesotelioma (cáncer de la pleura y otras membranas serosas). De tal manera, si en alguna zona geográfica existe un aumento significativo de la mortalidad por cáncer pulmonar y además del cáncer de vejiga, es posible sospechar que el agente causal de ambos es arsénico (en la Región de Antofagasta); si en alguna comuna existe alta mortalidad por cáncer pulmonar y mesotelioma, el agente causal de ambos sería asbesto; si sólo se produce una alta mortalidad por cáncer broncopulmonar y no por otros tipos de cáncer, es necesario que buscar otros posibles agentes causales.

Efectos diferidos por exposición prenatal tardía o infantil temprana por el mecanismo del imprinting epigenético

- En relación a la afectación de la salud generada por exposición perinatal a agentes ambientales por el mecanismo del imprinting epigenético, la Organización Panamericana de Salud en su reciente conmemoración de los 40 años de Alma Ata declara que en la actualidad, en el mundo, los bebés nacen pre contaminados por la exposición prenatal a químicos sintéticos y metales ambientales. Explicita específicamente del riesgo causado por la exposición en ciertas etapas del desarrollo a ciertos químicos, lo que por vías de imprinting epigenético se relaciona a una miríada de consecuencias para la salud, las que pueden manifestarse a lo largo de la vida de los individuos y ser potencialmente transmitidos a las generaciones siguientes. Y añade que esas exposiciones preconcepcionales y prenatales a químicos ambientales pueden y deben ser mitigados y prevenidos no solo por los cambios de hábitos de las personas, sino, por firmes medidas regulatorias tomadas por los gobiernos del mundo, esenciales para asegurar la salud futura de la población global (OMS, 2017; Poore et al., 2017; Sutton et al., 2012).

- Los efectos diferidos por exposición a agentes ambientales por el mecanismo de imprinting epigenético se refieren a los efectos irreversibles que causan numerosos agentes químicos que acceden al organismo durante la vida fetal tardía o durante los primeros años de la vida postnatal. Consisten en cambios irreversibles en la diferenciación de algunos tipos celulares que se encuentran en períodos críticos de su desarrollo, se manifiestan como alteraciones irreversibles en el número y/o calidad de algunos de sus receptores de hormonas o neurotransmisores, que ocurren durante los periodos críticos de su desarrollo o periodos ventana en los cuales ocurren las exposiciones a estos agentes; estos períodos ventana son de breve duración pero a tiempos diferentes para cada tipo celular, y en cada uno de éstos, para cada una de los diversos receptores de hormonas y neurotransmisores. Ocurren principalmente entre el sexto mes de la gestación y el segundo o tercer año de vida postnatal. Sus consecuencias que pueden detectarse en períodos más tardíos de la vida como desarrollo de enfermedades orgánicas o cambios neuroconductuales.

- El término “imprinting” fue acuñado por el biólogo húngaro G. Csaba, quién ha descubierto que la exposición prenatal o perinatal a niveles anormales de diversas hormonas o moléculas con actividad hormonal como el dietilestilbestrol, durante períodos críticos de la diferenciación celular, causa cambios irreversibles, que se mantienen de por vida, en las respuestas a diversas hormonas y la función de los tipos celulares afectados (Csaba & Nagy, 1976; Csaba, 1980; Dobozy et al., 1985; Csaba et al., 1986.). Esto sería causa del desarrollo de diversas enfermedades más tarde en la vida.

- El **primer efecto descrito en humanos** se refiere al desarrollo del adenocarcinoma cérvico-vaginal de células claras en mujeres jóvenes, causado por el tratamiento de sus madres durante su embarazo con el estrógeno sintético dietilestilbestrol (Herbst, 1981).

- **En Chile** se ha demostrado que **la exposición prenatal a arsénico** del agua potable de Antofagasta ha determinado un aumento de mortalidad por bronquiectasias y por EPOC en las edades de 30 a 49 años (Smith et al., 2006). De acuerdo a estos autores, se ha determinado un aumento en 46 veces de la mortalidad por bronquiectasias a las edades entre los 30 y 49 años para quienes nacieron de madres expuestas a casi 900 µg/L de agua potable, pero sólo 12 veces a los que nacieron de madres expuestas a alrededor de 100 µg/L, aunque los infantes hayan vivido expuestos posteriormente a casi 900 µg/L (Smith et al., 2006). La exposición prenatal y la infantil temprana a arsénico determina, más tarde en la vida, un aumento de la mortalidad por cáncer pulmonar y vesical, que se produce hasta 40 años después que se haya reducido la exposición a arsénico por el abatimiento del mismo del agua potable, lo que sugiere que la especie huma es notablemente muy sensible a dicho elemento durante sus primeros años de vida (Steinmaus et al., 2014). La exposición prenatal e infantil temprana a arsénico se ha traducido en un aumento importante de mortalidad adulta durante edades inferiores a 50 años (Smith et al., 2012), las causas de este aumento serán analizadas a continuación.

- Se ha descrito en Bangladesh una asociación entre exposición a arsénico durante la gestación y el aumento de enfermedades infecciosas durante la edad infantil, especialmente infecciones respiratorias bajas y diarrea (Raqib et al., 2009; Rahman et al., 2011, 2017). La inmunosupresión, que se produce en personas prenatalmente expuestas (Ahmed et al., 2011, 2012), sería el factor predisponente del aumento de riesgo de infecciones respiratorias y diarrea (Rahman, 2017), a través de una inhibición de la inmunidad celular (Ahmed et al., 2014) y humoral (Raqib et al., 2017). Sin embargo, no sólo las infecciones respiratorias serían los factores etiológicos de las alteraciones funcionales del aparato respiratorio. Las alteraciones de la metilación de los genes responsables de la remodelación de la matriz extracelular pueden desempeñar un papel importante que puede predisponer a enfermedades pulmonares más tarde en la vida (Gonzáles-Cortés et al., 2017). Dauphiné et al., 2011, demostraron que la exposición a temprana edad a arsénico proveniente del agua potable determinaba efectos irreversibles en el aparato respiratorio, que compararon en magnitud como similares a los que se produce en fumadores a través de la edad adulta. Recio-Vega et al. (2015) relacionaron la exposición pre- y perinatal a arsénico con una disminución de la función pulmonar en niños, y Ahmed et al. (2017) han sugerido que la

exposición prenatal a arsénico determina una función pulmonar alterada, y que en cambio la exposición infantil determina una reacción inflamatoria de vías aéreas, especialmente en niños varones.

- Uno de los mecanismos moleculares mejor conocidos del imprinting epigenético es la metilación del ADN de genes específicos, a través de lo cual se logra programar cuáles de los genes de cada tipo celular permanecerán activos durante toda la vida del individuo portador de dichos tipos celulares, y que este proceso ocurre en períodos "ventana" propios de cada tipo celular y que ocurren principalmente durante el último trimestre de la gestación y durante los primeros pocos años de vida postnatal (para una revisión, ver Tchernitchin et al., 2013). En el caso de la exposición perinatal a arsénico, en el ser humano, se demostró una asociación robusta de metilación del ADN en modelos de regresión lineal multivariada lineal, en la cual la exposición prenatal precoz a arsénico deprime la metilación del ADN en niños varones; esta asociación refleja una interferencia con una metilación de novo del ADN (Broberg et al., 2014). Trabajos posteriores han logrado establecer que los niveles de arsénico cuantificados en muestras de uñas podálicas maternas (tomadas alrededor del nacimiento de sus hijo(a)s), estaban asociados con la metilación de locus único CpG con altísima significancia estadística ($p = 4.1 \times 10^{-8}$), datos que demostraban el alto potencial del arsénico aun a niveles tan bajos como a los que se expone la población norteamericana, inducía metilación de genes específicos en placenta; este hallazgo apoya los nuevos mecanismos de acción del arsénico descritos para producir efectos a largo plazo después del nacimiento (Green et al., 2016). Otro estudio reciente demostró una asociación entre niveles de arsénico y la metilación de ADN de genes asociados con remodelación de la matriz extracelular pulmonar (*vide supra*, Gonzáles-Cortés et al., 2017), y una relación entre exposición prenatal a arsénico y el aumento de las concentraciones plasmáticas de IGFBP3 en niños de 9 años, mediada al menos parcialmente por metilación de ADN, que posiblemente esté relacionada con diabetes tipo 2 (Gliga et al., 2018).

- **En cuanto a efectos diferidos por exposición a agentes que tienen afinidad por receptores de la hormona estradiol (tomando en consideración que el nitrobenceno, identificado como uno de los contaminantes que afectaron Quintero-Puchuncaví, tiene afinidad y se une a estos receptores), existe la siguiente información:**

- Estudios realizados en la Universidad de Chile de exposiciones perinatales a hormonas androgénicas que interactúan con receptores de estrógenos perinatales en animales de experimentación indujeron el mecanismo

del imprinting, afectando en forma permanente respuestas a estradiol evaluadas en el útero de estos animales durante el periodo prepubertal. (Arriaza et al., 1989; Mena et al., 1992).

- La exposición prenatal a plomo en animales experimentales, determinan algunas secuelas permanentes que son opuestas a los efectos de exposición aguda, subaguda o crónica (Tchernitchin et al., 2003) a este elemento en animales juveniles o adultos, demuestra que los mecanismos de interacción son diferentes a los de toxicidad durante etapas posteriores de la vida (Tchernitchin et al., 2011). Efectos similares se han descrito en humanos por exposición a plomo a temprana edad.

- Los efectos diferidos por la exposición prenatal e infantil a anhídrido sulfuroso (dióxido de azufre) están descritos mas abajo (*vide infra*).

Efectos en salud por los contaminantes más prevalentes

1. Material particulado (MP2,5, MP10 y MPS)

El material particulado MP2,5 llega hasta los alvéolos y desde allí una parte de éste pasa directamente al torrente circulatorio, en donde causa una contracción de las arterias de mediano calibre (ejemplo, coronarias, arterias cerebrales), las que disminuyen en alrededor de un 40% de su diámetro. Si existen placas de ateroma que ocluyen parcialmente y asintomáticamente dichas arterias, esta contracción provocada por MP2,5 puede originar, 1 a 3 días después del episodio, su oclusión por un coágulo y el consiguiente infarto cerebrovascular o del miocardio circulatorio (Brook et al., 2002). El material MP10 por su diámetro no alcanza los alvéolos, es devuelto por el batido ciliar de los epitelios bronquiales hasta la glotis, en donde es deglutido y, una vez en el estómago, sus componentes bioaccesibles (por ejemplo, algunos metales pesados, arsénico, *vide infra*) son parcialmente solubilizados por la acción del ácido clorhídrico gástrico, y pueden ingresar al torrente circulatorio desde el intestino. Tanto el MP2,5 como el 10 causan inflamación bronquial y sus consecuencias son el desarrollo de infecciones respiratorias bajas (IRA bajas: neumonía, bronquitis) y crisis obstructivas. En la ciudad de Santiago se demostró (Ostro et al., 1966) que episodios de contaminación del aire con aumentos de valores de MP10 (entre el 50% y el 70% de este corresponde a MP2,5) causan un aumento de la mortalidad (en los 3 días siguientes al episodio) por enfermedades cardiovasculares y broncopulmonares a partir de 50 $\mu g/m^3$ N (índice ICAP 33,3), con un aumento de la mortalidad de al menos un 0,5% por cada 10 $\mu g/m^3$ N sobre 50 $\mu g/m^3$ N. De esta manera, con un índice ICAP 100 (150 $\mu g/m^3$), que es el límite legal entre aire bueno y regular, la mortalidad precoz aumenta en al menos 5%, es decir, si en la cuenca de Santiago sin contaminación fallecen 50 personas al día, con índice ICAP 100 fallecen al menos 2,5 personas en forma adicional. De la misma manera con índice ICAP 500, que define límite

entre preemergencia y emergencia (330 µg/m^3), la mortalidad diaria aumenta por lo menos un 14%, lo que se traduce en 7 muertes diarias evitables.

En cuanto a los efectos diferidos de la exposición crónica a material particulado, el efecto más notorio es aumento de la mortalidad por cáncer broncopulmonar (ejemplo, la mortalidad por cáncer pulmonar en la Región de Salud "Santiago Centro" era de 20/100.000 habitantes, mientras que en en la Región de Valdivia era 8,6 y el promedio país era 11,8 (Rivara & Corey, 1995).

Los diferentes efectos diferidos por exposición crónica están influenciados por la composición química de dicho material particulado.

Es necesario mencionar que el material particulado sedimentable (más grueso que el MP10) que de los bronquios o de las vías respiratorias superiores pasa a la glotis, es deglutido, y que la presencia de elementos bioaccesibles (en caso de los metales, aquellos que son solubles en el ácido clorhídrico pH 2,0 presente en el estómago) al ser solubilizados pueden entrar fácilmente al torrente circulatorio y causar sus efectos en los diversos órganos de la persona expuesta (Cortés et al.,2015; Tapia et al., 2018).

La exposición infantil durante los primeros años de vida, y la exposición prenatal (materna) causan efectos diferidos por el mecanismo del imprinting epigenético, que determina el desarrollo de enfermedades orgánicas o cambios neuroconductuales más tarde en la vida. Serán descritos a continuación de los elementos específicos descritos.

2. Efectos del SO_2 y sus derivados en humanos

2.1. Exposiciones controladas breves en voluntarios sanos. En el aparato respiratorio, el SO_2 por 10 minutos a 2.9-23 mg/m^3 aumenta la frecuencia cardíaca, disminuye el volumen respiratorio y aumenta la frecuencia respiratoria (Amdur et al., 1953). 2.9 mg/m^3 por 15 minutos causa un leve aumento de la resistencia respiratoria (Snell & Luchsinger, 1969). Una exposición de 1 a 3 horas a 2.9 mg/m^3 (1 ppm) de SO_2 disminuye el flujo de mucus nasal, el diámetro de la vía respiratoria nasal y obstaculiza el transporte mucociliar nasal (Andersen et al., 1974).

Aerosoles de ácido sulfúrico (0.35 mg/m^3 por 5-15 minutos) aumentan la frecuencia respiratoria y disminuyen el volumen respiratorio en el 33% de los voluntarios (Amdur et al., 1952).

Mezclas de SO_2 y ozono potencian el efecto producido por cada uno de estos compuestos por separado.

En estudios sobre actividad sensorial y la actividad de la corteza cerebral se demostró que los aerosoles de ácido sulfúrico en concentraciones que se perciben como olor o que causan irritación de membranas mucosas, causan una depresión

del sistema nervioso central. Desde niveles de 1.5 mg/m^3 de dióxido de azufre ó 0.73 mg/m^3 de aerosol de ácido sulfúrico se produce un retardo en el tiempo de los reflejos de origen visual (Bustueva, 1961). Las respuestas de adaptación a la oscuridad se afectan con 0,92 mg/m^3 de SO_2 ó 0,63 mg/m^3 de aerosol de ácido sulfúrico (Rjazanov, 1962). El ritmo alfa se suprime con 0,9 mg/m^3 SO_2 ó 0.63 mg/m^3 de aerosol de ácido sulfúrico (Bustueva et al., 1960). Los reflejos condicionados se afectan con 0,6 mg/m^3 de SO_2 ó 0.4 mg/m^3 de aerosol de ácido sulfúrico (Rjazanov, 1962).

2.2. Exposiciones controladas breves en sujetos asmáticos. En asmáticos que realizaban ejercicios algunos presentaban cambios en la función pulmonar y síntomas respiratorios tras exposición a SO_2 por10 minutos; esto motivó que la OMS concluyera que no se podía sobrepasar el nivel de 500 µg/m^3 durante 10 minutos (OMS, 2005). Niveles más altos de SO_2 desencadenan con mayor frecuencia crisis asmáticas. Por ejemplo, en un grupo de asmáticos el número de crisis incrementaba desde 1 hasta 4 por semana cuando la concentración de SO_2 incrementaba a 140-230 µg/m^3 y aumentaba a 12 por semana cuando los niveles de dióxido de azufre llegaban a 740 µg/m^3 (Yoshida et al., 1966).

2.3. Exposición ocupacional, especialmente industrial. Los trabajadores suelen estar expuestos a SO_2 y aerosoles de ácido sulfúrico, muchas veces asociado a otros contaminantes. La mayoría de los estudios sólo se han realizado en trabajadores empleados por esas industrias, y no en aquellos que han abandonado su trabajo en la industria para evaluar posibles efectos a largo plazo, incluyendo enfermedades, mortalidad y sensibilización a futuras exposiciones. En un estudio, la población expuesta se dividió en tres categorías: trabajadores de la planta industrial donde se localizará la fuente de emisión, los residentes adultos de los alrededores de la planta y los niños menores de 12 años. Los grupos de mayor riesgo son los niños y los trabajadores (Melgar et al., 2003).

2.4. Exposición comunitaria. La mayor parte de la información fue obtenida a partir de estudios epidemiológicos en a zonas geográficas con diferentes concentraciones de SO_2 (y de otros contaminantes) y poblaciones expuestas en forma aguda o prolongada. En trabajos previos, para exposiciones de corta duración a una combinación de SO_2 y material particulado total, las concentraciones menores (promedio de 24 horas) a las cuales se ha descrito efectos adversos eran para SO_2 200 µg/m^3 y para material particulado 150 µg/m^3. En exposiciones prolongadas a la combinación de ambos, concentraciones medias anuales de para SO_2 eran 60-140 µg/m^3, y para material particulado 100-200 µg/m^3. Se han descrito aumentos de mortalidad relacionados a niveles altos de contaminación con concentraciones promedio de 24 h del orden de 500 µg/m^3 (0,18 ppm) para dióxido de azufre y de 500 µg/m^3 para material particulado.

Entre las pruebas más recientes para fundamentar las recomendaciones 2005 de la OMS, se ha vinculado una reducción sustancial de enfermedades respiratorias en la infancia y de mortalidad en todas las edades a la reducción de azufre en combustibles, y no se obtuvo ninguna prueba de un umbral para los efectos en la salud con concentraciones de SO_2 durante 24 horas del orden de 5-40 µg/m^3. Los niveles de SO_2 durante 24 horas estaban significativamente asociados con las **tasas**

de mortalidad diaria en 12 ciudades canadienses en las que la concentración media era de sólo 5 µg/m^3 (el nivel medio más alto de SO_2 fue inferior a 10 µg/m^3) (Burnett *et al.*, 2004). En el estudio de la Sociedad Americana del Cáncer (AC S) se observó una asociación significativa entre el SO_2 y la mortalidad para la cohorte de 1982-1988 en 126 zonas metropolitanas de los Estados Unidos en las que la concentración media registrada de SO_2 era de 18 µg/m^3 y la media más alta de 85 µg/m^3(Pope *et al.*, 2002). En caso de que hubiera un umbral para los efectos en cualquiera de estos estudios, tendría que ser muy bajo, según la OMS (2005), que recomendó para 24 horas como enfoque precautorio prudente un valor de 20 µg/m^3. Si se respeta el nivel de 24 horas, se garantizan unos niveles medios anuales bajos. Estos valores guía de la OMS (2005) para el SO_2 no están vinculados a los del material particulado.

Los estudios de los efectos de exposiciones muy breves (10 minutos) a concentraciones bajas de SO_2 en niños asmáticos, que detectaron cambios en la función pulmonar y síntomas respiratorios, también avalan las nuevas recomendaciones de la OMS (2005) en las que no se debe sobrepasar el nivel de 500 µg/m^3 durante 10 minutos.

Mortalidad aguda: Los episodios históricos que más claramente demostraron aumentos de mortalidad como consecuencia de exposición a altos niveles de óxidos de azufre fueron: en el Valle del Meuse, Bélgica, en 1930 (Firket, 1931); en Donora, Pennsylvania, USA, en 1948 (Schrenk et al., 1949), y en Londres, Gran Bretaña, en 1952 (Ministry of Health, United Kingdom, 1954). En el episodio de Londres ocurrieron 4000 muertes en exceso sobre los esperados durante un episodio de contaminación del aire que duró 5 días. Posteriormente se propuso que la mortalidad aumenta cuando la concentración de material particulado aumenta a más de 100 µg/m^3, o la concentración de dióxido de azufre aumenta sobre 70 µg/m^3.

Entre las últimas pruebas de que se disponía para fundamentar las recomendaciones 2005 de la OMS, figura un estudio realizado en Hong Kong en el que se ha vinculado con una reducción sustancial de los efectos en la salud (mortalidad en todas las edades, enfermedades respiratorias en la infancia) con una reducción sustancial del SO_2.(Hedley *et al.*, 2002). **Los niveles de SO_2 durante 24 horas estaban significativamente asociados con las tasas de mortalidad diaria en 12 ciudades canadienses donde la concentración media era sólo 5 µg/m^3** (el nivel medio más alto fue inferior a 10 µg/m^3 SO_2) (Burnett *et al.*, 2004).

Mortalidad – efecto de exposiciones prolongadas. Se describió una mejor correlación con mortalidad cuando se correlacionaba las muertes con los niveles de contaminación ocurridos con 10 años de anterioridad (Gardner et al., 1969). Estos hallazgos ilustran que **los factores más relevantes no eran la contaminación reciente, sino aquella ocurrida más tempranamente en la vida**. Esto demuestra que exposiciones previas sensibilizan a los expuestos a que los afecte con más intensidad exposiciones futuras. Esto también **explica la intensidad de los síntomas en niños y adultos**

afectados con las concentraciones de SO_2. y de otros contaminantes asociados en La Greda y en otros lugares de la Región.

Recientemente se ha demostrado que **la pobreza potencia el efecto adverso en salud del dióxido de azufre** (Wong et al., 2008)**.**

Morbilidad – efecto de exposiciones breves. Se han demostrado correlaciones entre niveles de sulfato en el aire y enfermedades respiratorias (Dohan & Taylor, 1960). Una mejor correlación se encontró durante una epidemia de influenza (Dohan, 1961).

Cuando se redujeron significativamente los niveles de contaminación, persistía la correlación entre las condiciones de salud de los pacientes y las concentraciones diarias de SO_2 y de material particulado.

Los síntomas de irritación aumentan a partir de 310 µg/m^3 (0,11 ppm) de dióxido de azufre, de 145 µg/m^3 de material particulado total, y de 6,6 to 7,6 µg/m^3 de sulfatos totales (Cohen et al., 1974). Los valores de funciones pulmonares en pacientes adultos residentes en ciudades holandesas eran superiores en años de menor contaminación con SO_2 (45-100 µg/m^3) y material particulado (15 a 40 µg/m^3), que en los mismos pacientes años con valores más altos de estos contaminantes en el aire (120 a 300 µg/m^3 y 15 a 140 µg/m^3 respectivamente). Esa diferencia no fue detectada en pacientes de zonas rurales (Van der Lende et al. 1975).

Se ha demostrado que la inhalación de esos microcristales de sulfato (que se forman a partir del SO_2), desencadenando infartos de miocardio, la mayoría masivos y mortales (Brook et al., 2002; Pope et al., 2002).

Morbilidad – efecto de exposiciones prolongadas. En varones de 40 a 59 años de edad la prevalencia de bronquitis era mayor en áreas en donde el índice de sulfatación era mayor (Tsunetoshi et al., 1971). Se comparó los efectos de vivir en áreas con menor contaminación (dióxido de azufre 45 µg/m^3 y material particulado 90 µg/m^3) con aquellos en áreas más contaminadas (SO_2 125 µg/m^3 y material particulado 170 µg/m^3), en estas últimas aumentaba la frecuencia de síntomas respiratorios y las funciones respiratorias eran más deficientes. En áreas menos contaminadas el 11% de los residentes presentaban bronquitis y el 5% asma bronquial, a diferencia de áreas más contaminadas con un 19% de la población con bronquitis y un 11% con asma bronquial (Sawicki, 1972).

Hay factores que modifican efectos en salud del SO_2. La exposición a SO_2, al igual a la de otros contaminantes, causa alteraciones en salud más pronunciadas a los sectores de menores recursos económicos y afecta en menor grado a los de mejor nivel social (Wong et al., 2008). Eso significa que la pobreza potencia los efectos adversos en salud del dióxido de

azufre y de otros contaminantes ambientales. Las bajas temperaturas también potencian los efectos adversos del SO_2 (Kan et al., 2010). Algunas sales de metales (ejemplo **manganeso)** catalizan la transformación del SO_2.a aerosoles de ácido sulfúrico, **agravando los efectos en salud. Algunos aerosoles metálicos y otros contaminantes también potencian los efectos en salud del SO_2 y de sus subproductos, sulfatos o aerosoles de ácido sulfúrico** (analizado más arriba).

Morbilidad infantil. Se ha demostrado una **correlación entre frecuencias de infecciones respiratorias bajas y niveles de contaminación con SO_2.** En un posterior seguimiento de estos niños, a la edad de 20 años (Colley et al., 1973), los síntomas respiratorios estaban principalmente relacionados a los hábitos tabáquicos, no obstante, también había una **relación entre la prevalencia de los síntomas y las historias previas de infecciones respiratorias bajas las que, a su vez, estaban relacionadas con la contaminación estimada durante la infancia**. **Eso evidencia que la exposición infantil a SO_2 condiciona la frecuencia de enfermedades respiratorias más tarde en la vida**. Además se ha descrito que **en niños la exposición crónica a SO_2 deja secuelas negativas en diversos parámetros respiratorios** (Grosser et al., 1971)**.**

También hay una asociación de exposición crónica a SO_2 con **la faringitis crónica acompañada de cambios histopatológicos en las biopsias, conjuntivitis aguda y crónica** y se han descrito **efectos en recuentos de células sanguíneas**, en las **amígdalas** y **nódulos linfáticos cervicales**, **retardo del crecimiento y osificación** e **hipocromía eritrocitaria** (Maziarka & Mróz, 1968; Melgar et al., 2003).

En residentes de zonas con contaminación con SO_2 de origen industrial, **los niños menores de 12 años constituían**, al igual que los trabajadores de la empresa emisora de SO_2, **los grupos de mayor riesgo**. También se encontró una **relación entre incrementos de SO_2 en el aire y un aumento de hospitalizaciones por enfermedad reumática infantil**. (Vidotto et al., 2012).

Cáncer pulmonar. Numerosos estudios determinaron una **relación entre contaminación con material particulado y dióxido de azufre con el cáncer pulmonar**. Los primeros estudios atribuyeron el aumento del cáncer pulmonar al material particulado y a la presencia de benzo(a)pireno en éste. Más tarde se determinó que el papel del SO_2 en la patogénesis del cáncer pulmonar se basa en resultados experimentales en donde la **exposición a SO_2 aumenta el poder carcinógeno del benzopireno** y que la exposición a material particulado fino constituido por **sulfatos (estos últimos provenientes del SO_2) favorece el desarrollo de cáncer pulmonar**. (Stocks, 1966; Skvorcova et al., 1973; Pope et al., 2002).

Efectos diferidos e irreversibles por el mecanismo del imprinting de la exposición prenatal tardía o infantil precoz a compuestos de azufre. El imprinting o alteración de la programación celular se refiere al efecto irreversible que causan numerosos compuestos químicos que acceden al organismo durante la vida fetal tardía o durante los primeros años de la vida postnatal.

De acuerdo a proposiciones del Dr. Tchernitchin (Tchernitchin & Tchernitchin, 1992; Tchernitchin et al., 1999, Tchernitchin et al, 2013, Tchernitchin & Gaete, 2015), para la Organización Mundial de la Salud el origen de numerosas enfermedades que afectan a los adultos puede ser atribuido, al menos en parte, a la exposición prenatal o infantil temprana a diversos agentes inductores de imprinting epigenético, en especial contaminantes ambientales. Entre ellos, está demostrado el efecto de exposición perinatal a diversos metales pesados (plomo, arsénico, cadmio, mercurio), ozono, monóxido de carbono, dióxido de nitrógeno, benzopireno y otros contaminantes.

Se ha demostrado en ratones que la **exposición prenatal a dióxido de azufre induce cambios neuroconductuales que se manifiestan durante la edad adulta** y que limitan aquellas conductas que significan defensa en situaciones de peligro.

En otro estudio se demostró que la exposición prenatal a aire contaminado causó una deficiencia en la capacidad de defensa antioxidante en los eritrocitos que ha persistido hasta la edad adulta, con menores actividades de catalasa, superoxido dismutasa y glutatión peroxidasa. Además se redujo el peso corporal de los animales.

Imprinting - hallazgos en humanos: Hay evidencia epidemiológica que la exposición materna a contaminación ambiental, en especial material particulado (que en parte importante contiene sulfatos) afecta el desarrollo fetal**, causando bajo peso al nacer**. Se demostró una asociación estadísticamente significativa entre bajo peso al nacer y exposición prenatal (durante el tercer trimestre del embarazo) a SO_2, y que el efecto variaba de acuerdo al grupo étnico (Gardner et al., 1969). Existe también evidencia de una asociación entre las exposiciones prenatal o durante el primer año de vida a SO_2 (y también a otros contaminantes del aire en forma independiente al dióxido de azufre) y el **desarrollo de asma bronquial más tarde en la vida**. También se ha demostrado que la **residencia en lugares cercanos a fuentes puntuales de emisión industrial estaban asociados a desarrollo de asma bronquial más tarde en la vida.**

> **Nota:** Hay una descripción exhaustiva de los efectos en salud del arsénico y de los productos de oxidación del azufre, en un informe enviado por el Dr. Tchernitchin a la Corte de Apelaciones de Valparaíso fechado 27 de diciembre de 2012 y enviado los primeros días de enero de 2013 (**RUC 1100309960 3**).

3. Arsénico

La exposición humana crónica a arsénico determina un aumento de mortalidad por cáncer broncopulmonar (en Antofagasta 36/100.000 habitantes, en vez de 8,6 en Valdivia o 11,8 promedio país), de la vejiga (en Antofagasta 10,6 en vez de 0,8 en Valdivia, 1,7 promedio país) y renal (6,6 en Antofagasta, en vez de 3,3 en Valdivia y 2,6 promedio país) (Rivara & Corey, 1995). También determina un aumento de riesgo de desarrollar cáncer renal, de vías urinarias, hepático y de piel. Aumenta la mortalidad por infartos del miocardio (Navas-Acien et al., 2005), incluso en personas jóvenes, y puede causar el Síndrome de Raynaud. Numerosos trabajos demuestran la relación de la exposición crónica a arsénico y desarrollo de algunos cánceres (Mostafa et al., 2008; IARC, 2010).

La exposición prenatal a arsénico o infantil temprana puede determinar efectos diferidos mediados por el mecanismo del imprinting epigenetico, y que están descritos más arriba.

La exposición a arsénico durante los primeros 4 meses de la gestación determina un aumento de abortos espontáneos y de reabsorciones fetales (Nordström et al., 1978), y de malformaciones fetales renales y del sistema nervioso (Nordström et al., 1979).

Nota: Hay una descripción exhaustiva de los efectos en salud del arsénico y de los productos de oxidación del azufre, en un informe enviado por el Dr. Tchernitchin a la Corte de Apelaciones de Valparaíso fechado 27 de diciembre de 2012 y enviado los primeros días de enero de 2013 (**RUC 1100309960 3**).

4. Contaminantes ambientales identificados EN EL EPISODIO DE AGOSTO-SEPTIEMBRE de 2018 (Quintero-Puchuncaví).

Efectos en salud por exposición a los agentes químicos informados inicialmente
Sólo nos referiremos a tres de los primeros compuestos. No se han descrito en la literatura científica efectos adversos del isobutano a las concentraciones en las que pudo encontrarse en Quintero, por lo cual se espera que no ocurran consecuencias adversas por la presencia de este hidrocarburo.

1. **El Nitrobenceno** en forma aguda o subaguda causa metahemoglobinemia, lo cual al dificultar el transporte de oxígeno desde los pulmones a los tejidos produce anoxia tisular, afectando principalmente el sistema nervioso

central y el riñón. Produce apoptosis neuronal (muerte celular programada) (Seyfried & Wüllner, 2007) y, aún, a menores concentraciones causa efectos neurológicos, como aquellos detectados en el Hospital de Quintero. Causa una inflamación intestinal intensa, afectando principalmente el colon (intestino grueso), explicando la diarrea, y también los vómitos (Araújo et al., 2017). En concentraciones más altas causa daño cromosómico (del ADN) (Baig, 2016). Es un carcinógeno para diversos órganos y en especial causa leucemia (Baig, 2016). Se une a receptores de hormonas esteroidales, especialmente estrógenos (Baig, 2016), lo cual significa que está involucrado en el mecanismo del imprinting epigenético; es decir, exposiciones durante periodos ventana entre los últimos 3 meses de la gestación humana y el segundo o tercer año de vida postnatal causan cambios en los programas de diferenciación de diversos tipos celulares para definir el número y calidad de receptores de hormonas y de neurotransmisores de por vida. Su alteración causada por este mecanismo determina una alta probabilidad de desarrollo de enfermedades orgánicas y cambios neuroconductuales más tarde en la vida (Tchernitchin et al., 2013; Tchernitchin & Gaete, 2915).

2. **El Metil Cloroformo** en forma aguda produce somnolencia. En más en altas concentraciones produce cefalea, náuseas, vómitos, diarrea y mareos, y en concentraciones muy altas puede producir pérdida de conocimiento y aún la muerte. La exposición crónica causa daño hepático y afecta las funciones cardíacas, además de afectar la piel y el aparato digestivo. La exposición crónica en el largo plazo afecta las funciones cardíacas, aumenta el riesgo de cáncer hepático y reduce los años de vida (Stewart, 1971; ATSDR, 1995; HSDB, online database, 1993; Sitting 1985; EPA/600/8-82-003, 1982; RTECS, online database, 1993). Aún cuando no hay publicaciones científicas respecto de los efectos diferidos por exposición prenatal o infantil a dicho compuesto a través del mecanismo del imprinting epigenético, su estructura química (tres átomos de cloro y un radical metilo unidos al Carbono-1) sugieren un posible efecto similar al de los policlorobifenilos (PCB).

El uso de metilcloroformo (tricloroetano) en Chile está prohibido desde el año 2015, en virtud del acuerdo del Protocolo de Montreal (1987), que ha sido firmado por Chile. En consecuencia, es obligación cumplir con lo que nuestro país se ha comprometido en materia de acuerdos internacionales. **Incumplir con ese compromiso es una infracción extremadamente grave.** Los países desarrollados se comprometieron eliminar su uso hacia 1996, y los países en vías de desarrollo hacia 2015. Por otra parte, es necesario que la ciudadanía tenga conocimiento que, según nuestras leyes, en Chile NO HAY DELITOS AMBIENTALES. Por lo cual, en Chile se opera en total impunidad sin responsabilidad legal ulterior para quienes causaron episodios como los ocurridos (Krol, 2003).

3. **El Tolueno.** Se han reportado efectos diferidos por exposición prenatal a tolueno (ver revisión en Tchernitchin, 2005). En madres gestantes por exposición ocupacional materna se ha descrito un aumento de abortos espontáneos (Jones & Balster, 1998). En hijos de madres que utilizaban tolueno como droga de abuso durante la gestación (exposición prenatal) se ha descrito retardo del crecimiento, déficit cognitivo, de lenguaje y motor, déficit intelectual, microcefalia, malformaciones craneofaciales (Hersh, 1989; Arnold et al., 1994; Jones & Balster, 1998), y en casos de muerte del recién nacido, atrofia cerebral (Arai et al.1997).

Proposiciones generales

1. Instalación de diversos equipos de monitoreo, con capacidad para medir todos los gases tóxicos, material particulado y otros componentes tóxicos, normados o no, que las empresas emiten al ambiente, de manera continua o frecuente, operados por personal capacitado y sin conflicto de interés (ya sea municipal o dependiente del Ministerio de Salud) o especializado, a través de entidades externas, con metodologías auditables. Debe existir comunicación pública, diaria, de los rangos de variación de cada contaminante, en valores absolutos y no promedios (nombre del compuesto, valores mínimos, máximos y horarios en que se producen las mayores concentraciones), todos medidos durante las 24 horas del día.

2. **Homologar las normas actuales de la OMS vigentes como normas aplicables legalmente en Chile, para todos los contaminantes emanados por las actividades antropogénicas en las comunas de Quintero, Puchuncaví y Concón. Nos referimos a normas para calidad de aire, agua potable, aguas de riego, aguas recreacionales e igualmente para suelos. Igualmente, las normas de aguas para diversos usos y las normas de suelo vigentes de la OMS y/o de los países más exigentes deberán homologarse para tener fuerza legal obligatoria en Chile. Para realizar esto se sugiere dictar un Decreto Supremo, a partir de la potestad reglamentaria autónoma del Presidente de la República.**

3. Suspensión y/o condicionalidad de funcionamiento y permisos industriales ya otorgados, supeditados al cumplimiento de las nuevas normas homologadas (OMS) con validez legal en Chile.

4. Paralización, inmediata, de nuevos permisos a nuevas fuentes que contribuyan a empeorar la actual situación de saturación de emisiones, en la V región.

5. Actualización toxicológica de toda la población expuesta, con delimitación y clausura de los lugares contaminados y su prohibición de uso para todo fin, hasta la descontaminación total del suelo e instalaciones.

6. Instalación de un Consultorio de Salud, en Quintero, especializado en Contaminación, con medios instrumentales y personal capacitado para enfrentar emergencias industriales

7. Descontaminación del suelo, aire y aguas de las zonas contaminadas, bajo los nuevos estándares normativos de exigencias con validez legal. Este proyecto de descontaminación deberá ser financiado, en partes iguales, entre las empresas del complejo industrial y el Estado que las ha autorizado a operar. Informar, avances de manera paralela al PRAS (Programa para la recuperación ambiental y social) de Quintero, Puchuncaví y Concón.

8. Acelerar la re-conversión de todas las industrias y las plantas a energías no contaminantes[1], dando de baja y reemplazando actuales fuentes de contaminación obsoletas por ERNC[2], estipulando una fecha máxima para cumplir con esta reconversión, sino aplicar sanciones drásticas por incumplimiento.

9. Desarrollo de Planes de Descontaminación de todas las zonas contaminadas, suelos, mar, costa, playas, aguas, entre otros, con financiamiento compartido entre las empresas que han contaminado y el estado de Chile que lo ha permitido, al incumplir sus obligaciones constitucionales. Existen estudios publicados por Ministerio de Medio Ambiente en el año 2013 y por IFOP en el año 2016, donde se alertaba que la fauna marina de la bahía bioacumulaba metales, con riesgo potencial para el consumo humano. Se debe dar cuenta, públicamente, del avance del proceso de descontaminación, en todas las zonas donde se haya afectado la cadena alimentaria.

10. Establecimiento de un Consultorio de Salud Ambiental, en donde se establezca una metodología científica para la atención adecuada de la población que ha sido expuesta durante decenios a tóxicos dañinos para la salud. Este consultorio especializado en Contaminación y Salud deberá tener el presupuesto adecuado para contar con medios, instrumental y personal capacitado para enfrentar emergencias industriales.

[1] Del mismo modo como lo están haciendo en sus países de origen (Ej. AES Gener)

[2] y adecuar la Planta ENAMI Ventanas a estándares internacionales en cuanto a procedimientos.

11. Dictación de una ley similar a la de los polimetales de Arica, para asegurar, de por vida, la futura atención en salud de todos los habitantes de las Comunas de Quintero y Puchuncaví, por secuelas al haber sido expuestos crónicamente (cáncer) y/o perinatalmente a los diversos contaminantes del parque industrial actual.

Proposiciones para la emergencias

12. **Evacuación de toda la población infantil y mujeres embarazadas de las zonas afectadas** cuando se produzcan emergencias sanitarias definidas de acuerdo a orientaciones internacionales. Es preocupante la situación de mujeres embarazadas y por lo menos a menores de 2 años (siendo preferible incluir también niños de edades superiores) por los daños irreversibles casados por el mecanismo de imprinting epigenético descrito as arriba. Esta evacuación deberá ser voluntaria, pero debe proveerse del transporte y alojamiento necesarios. También es necesario TENER CONSIDERADA LA SITUACIÓN DE GRUPOS VULNERABLES (enfermos del sistema cardiovascular y/o respiratorio, crónicos).

13. Para eventos de emergencia sanitaria La **ONEMI a nivel nacional debe convocar y coordinar las actividades de las diferentes entidades implicadas en la institucionalidad ambiental y laboral**, que están llamadas a cumplir su rol en la prevención de emergencias de este tipo. Incluyendo en esto a los organismos relacionados con la prevención de riesgos industriales y organismos fiscalizadores. Esta coordinación debe hacerse con mecanismos de transparencia y de participación de la comunidad.

14. Crear un plan de emergencia química en esta zona, para rescate del personal en las plantas industriales y para rescate de la población afectada, coordinando con los hospitales de la zona y de otros lugares la eficiente atención a los pacientes, probado con simulacros (Plan Daisy).

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4. http://dehesa.unex.es/bitstream/handle/10662/6136/TDUEX_2017_Salmani_Ghabeshi.pdf?sequence=1&isAllowed=y

2. Observaciones al Inventario de Emisiones
Nombre: Andrei N Tchernitchin (Andrés Tchernitchin Varlamov) Jerarquía/cargo: Presidente, Departamento de Medio Ambiente del Colegio Médico de Chile, Profesor Titular U de Chile, Postdoctoral Fellow Population Council University of North Carolina & University of Pennsylvania Depto M.A. Colegio Médico de Chile Observaciones: El inventario de emisiones para MP2,5 y 10 está bien, pero para los COV no está bien identificado en especial en el Complejo Industrial Ventanas. De Codelco Ventanas se informa el MP y el SO2, pero no hay información sobre arsénico. Enap (supongo que refineria en Concón) se informa PM, SO_2 y NO_x, pero falta informacion sobre COV. No hay información sobre los diversos COV. Como se ha evaluado la reducción de morbilidad mortalidad si no han considerado el As, el benceno, el Xileno y otros compuestos carcinógenos? Como se evaluan los otros agentes tóxicos emitidos por AESGENER?

3. Observaciones al Informe de la SEREMI de Medio Ambiente
Nombre: Andrei N Tchernitchin (Andrés Tchernitchin Varlamov) Jerarquía/cargo: Presidente, Departamento de Medio Ambiente del Colegio Médico de Chile, Profesor Titular U de Chile, Postdoctoral Fellow Population Council University of North Carolina & University of Pennsylvania Depto M.A. Colegio Médico de Chile Observaciones:

1. Llama la atención que la empresa Oxiquim no ha sido siquiera mencionada en el inventario de emisiones ni se ha investigado la hipótesis que esta empresa haya emitido algunos de los compuestos invstigados en la crisis sanitaria de agosto – octubre 2018.
2. El inventario de emisiones supuestamente más importantes emisiones se refieren principalmente a material particulado respirable (MP10), material particulado fino respirable (MP2,5) y sus precursores tales como dióxido de Azufre (SO2), óxidos de nitrógeno (NOx) y compuestos orgánicos volátiles (COVs); no hay mención del arsénico y metales pesados, de compuestos orgánicos volátiles de los cuales algunos compuestos específicos pueden ser los causantes de la actual crisis, ni de otros compuestos toxicos que afectan la salud y que pueden ser emitidos por diversos procesos industriales del Coplejo Industrial, de los cuales algunos no son parte de la composición natural del petróleo (nitrobenceno, tricloroetano), hidrocarburos policíclicos aromáticos, benzopireno, policlorobifenilos, dioxinas, entre otros.
3. Ministerio de Medio Ambiente a través del D.S. N°10 declara zona saturada por material particulado fino respirable MP2,5, como concentración anual y latente como concentración diaria, y zona latente por material particulado respirable MP10, como concentración anual, las comunas antes mencionadas. Excluyendo el SO_2, las concentraciones de material particulado y óxidos de nitrógeno no difieren mucho de lo que ocurre en la Cuenca de Santiago. Incluso se menciona que tienen una tendencia a mejorar. Entonces **¿por qué se produce la crisis sanitaria y ambiental de la zona?** Si el plan de descontaminación tiene el objetivo de volver a las normas que regulen solamente los contaminantes que están reguilados (MP10, MP2,5 y SO_2), lo cual es positivo, pero no se puede decir públicamente que va a solucionar el problema de las crisis sanitarias que han ocurrido últimamente. Eso significa dar falsas esperanzas a la población. Aún cuando significa que el intento de reducir los agentes mencionados en el plan es útil, pero **el plan no sirve realmente para solucionar los verdaderos problemas de la zona ya que los agentes causantes son otros y son más peligrosos**.
4. En resumen, lo propuesto mediante la Resolución Exenta N° 907 del 2 de octubre del 2018, el Ministerio de Medio Ambiente que da inicio a la elaboración del nuevo Plan de Prevención y de Descontaminación Atmosférica para las comunas de Concón, Quintero y Puchuncaví (PPDA), no es el adecuado para enfrentar la emergencia sanitaria y ambiental.
5. Las normas primarias para material particulado MP10 y 2,5, tanto anuales como diarias, son mucho más permisivas que las recomendadas por la OMS y adoptadas por numerosos países. El plan de descontaminación debería regular las emisiones para llegar en un tiempo más breve (3 años) cuplir con las normas nacionales, pero debe quedar establecido que en un plazo adicional de 3 años deben cumplirse las recomendaciones de la OMS. Lo mismo para los otros contaminantes atmosféricos.

6. Debe establecerse una norma primaria para arsénico, y entonces regular las emisiones máximas (especialmente fundición Codelco Ventanas) de arsénico.
7. La Contraloría General de la República, que mediante Oficio Nº 44528, de 26 de diciembre de 2017, representó el D.S. Nº 1 aludido en la letra h), por no ajustarse a derecho, señalando que el plan aprobado no cumplía con la finalidad que la normativa le asigna, dado que las medidas dispuestas en el mismo no permitían una efectiva reducción de los contaminantes. Por lo mismo, reducciones leves a las emisiones podrán ser rechazadas puesto que no contribuirán significativamente a los objetivos que debe tener un plan de descontaminación.
8. El 21 de agosto de 2018, producto de la presencia de contaminantes en la zona de Quintero y Puchuncaví, se vieron afectadas al menos 82 personas, que presentaron uno o más síntomas de náuseas, vómitos, odinofagia, molestias oculares, otalgia, cefalea, dolor torácico, disnea, taquicardia o bradicardia, mareos y desvanecimiento, entre otros (**¿por qué no se mencionan aquí los síntomas y signos neurológicos?**). Los síntomas anteriormente descritos se asociaron a la presencia de emisiones de contaminantes en la zona. Con fecha 23 de agosto de 2018, después de un nuevo evento de presencia en el aire de contaminantes, que produjo 180 atenciones de salud, las autoridades pertinentes declararon alerta amarilla en la zona y que con fecha 4 de septiembre, un nuevo evento de las características indicadas en la zona tuvo como consecuencia más de 155 consultas, producto de dolores de cabeza, malestar estomacal, náuseas, entre otros síntomas. Al 12 de septiembre de 2018, se habían presentado un total de 792 consultas de salud asociadas a los hechos descritos precedentemente, 14 de las cuales han resultado en hospitalizaciones y 5 pacientes han experimentado síntomas neurológicos. **Los síntomas y signos neurológicos han sido detectados en más que 5 pacientes**. **El plan no aborda los compuestos que pueden generar esos síntomas neurológicos ni los de vómitos y diarrea intensos, que corresponden a los efectos del nitrobenceno. La cefalea causada por nitrobenceno es también un síntoma neurológico. Si estos compuestos no son considerados, la ejecución del PPDA no va prevenir futuras crisis sanitarias.**

4. Observaciones al AGIES

4.1. Antecedentes

Nombre: Andrei N Tchernitchin (Andrés Tchernitchin Varlamov)

Nombre: Andrei N Tchernitchin (Andrés Tchernitchin Varlamov)
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Depto M.A. Colegio Médico de Chile
Observaciones:

4.2. Metodología del AGIES

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Depto M.A. Colegio Médico de Chile
Observaciones:

4.3. Evaluación de medidas

Nombre: Andrei N Tchernitchin (Andrés Tchernitchin Varlamov)
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Depto M.A. Colegio Médico de Chile
Observaciones:

I. UTILIZACION INADECUADA DEL PLAN DE PREVENCION Y DESCONTAMINACION PARA EL CONTENIDO PRESENTADO

Existen una serie de falencias, omisiones e incongruencias en el PPDA presentado para lograr los objetivos que ameritan y justifican su existencia:

1. Prevenir, eficaz y eficientemente, episodios de contaminación con impacto en la salud y

2. Descontaminar, eficaz y eficientemente, la contaminación existente en el ambiente: aire, suelo y aguas, para evitar seguir imponiendo riesgos de salud en la población y en la biodiversidad

Por lo tanto, el PPDA presentado no puede denominarse Plan de Prevención ni puede denominarse Plan de Descontaminación ambiental, con el objetivo de minimizar los efectos en la salud y la biodiversidad de las localidades afectadas.

A continuación se fundamenta lo anteriormente mencionado:

No se definió un Plan de Prevención de episodios que afectan a la salud de la población de las localidades afectadas (y su biodiversidad)

Para que el plan de prevención de episodios de contaminación, que impactan la salud de las personas, tenga resultados objetivos y medibles, se deben definir al menos los siguientes pasos básicos, omitidos en el plan:

1. Definir nuevas normas de calidad primaria, ajustadas al menos a lo que la OMS recomienda, para los contaminantes normados en la actualidad. Adicionalmente, definir normas de calidad primaria y secundaria, para todos los compuestos no normados que afectan al ambiente. Es decir, si la OMS no tiene norma definida para la mayoría de compuestos, el MINSAL junto al Colegio Médico de Chile la deben definir, al más breve plazo.

2. Instalar equipos de medición de contaminantes para todo el espectro de gases y contaminantes que afecten el aire, suelo y aguas, que las empresas emiten, normados o no, alrededor de cada empresa y en los puntos de emisión. Además, se deben instalar múltiples equipos de medición en zonas sensibles (colegios, hospitales, parques, zonas concurridas), entregando esa información en línea, en un sitio del MMA o del Ministerio de Salud, que sea transparente para las comunidades. La evaluación e implementación de estas medidas debe llevarse a cabo en un plazo de dos meses, que es lo máximo que puede tardar en quedar funcionando todos los sistemas a adquirir, con equipos de profesionales independientes encargados por cada localidad.

3. Definir la paralización del funcionamiento de plantas que infrinjan las nuevas normas de calidad primaria y secundaria y definir multas muy elevadas a las empresas que las sobrepasen. Es responsabilidad de las empresas contar con los mecanismos y sistemas de neutralización o reconversión de emisiones, al más breve plazo.

4. Integrar la salud como factor crítico en la Evaluación Ambiental Estratégica de proyectos, pasados y futuros (hasta ahora ausente para las autoridades). Bajo lo cual se deben revisar todos los procesos de operación autorizados en el pasado y los nuevos bajo nuevas restricciones.

5. Fortalecer a la ONEMI en la preparación de emergencias que afecten a la salud, integrando equipos de profesionales técnicos para resolver, de inmediato, el tipo de contaminante y su concentración que ocasiona los cuadros de salud de la población.

6. Definir programas de capacitación en diversos niveles:

Operarios y Supervisores de plantas industriales, para entender de mejor forma, lo riesgos de no seguir procedimientos operacionales.

Alumnos, profesores, padres y apoderados, para conocer y distinguir síntomas tempranos en niños con problemas en el colegio de cualquier tipo. Pues, existen agentes tóxicos que permanentemente, pueden ocasionar síntomas sobre tod en niños.

Comunidad, para prepararlos en caso de emergencias químicas y donde comunicar casos de observación de infraacciones a las nuevas normas, que las empresas deben cumplir. Cuál es el procedimiento para que la comunidad denuncie riesgos para prevenir incendios cercanos a desechos tóxicos o explosiones o contaminación que afecte a la salud, para que se actue de inmediato en la emergencia, entre otros temas.

Es muy importante que al más breve plazo el nuevo plan de prevención contemple al menos los puntos enunciados. Pues, diariamente, se está afectando la salud de las personas y la biodiversidad de cada una de las localidades y existe la forma de minimizarla, a corto plazo.

Basados en que los puntos anteriores para prevenir episodios de contaminación con impacto en la salud de las personas, al revisar el PPDA propuesto observamos que se han omitido todas las medidas básicas enunciadas. Pues, el PPDA presentado

tiene como objetivo disminuir las normas de emisiones, sin considerar el impacto en la salud de las personas o el deterioro a la biodiversidad. Por lo tanto, posee una serie de falencias, omisiones e incongruencias que **se explican con mayor detalle en la sección 4.5, ANEXOS**.

No se definió un Plan de Descontaminación para el aire, suelo y aguas de las localidades afectadas, sino que se usa la palabra descontaminación como sinónimo de contaminar menos

Sin definir, explícitamente, las normas de calidad primaria y secundarias, para cada uno de los compuestos contaminantes del ambiente emitidos por cada una de las empresas de los cordones industriales, no se puede elaborar un plan de descontaminación, pues se desconoce el valor objetivo que se pretende alcanzar, para proteger la vida humana y la biodiversidad.

Por otra parte, la contaminación del aire, suelo, mar, aguas de riego que afectan la salud humana y la biodiversidad debe ser identificada y medida, al más breve plazo, en cada localidad. Para ello, se requiere de equimamiento de medición, de última generación, y personal especializado en su operación, lo cual es factible de realizarse en muy corto plazo. Cada localidad posee amplias zonas acopios, sectores a alta contaminación en el mar y en lugares de cultivos agrícolas, que siguen acumulando contaminantes, que deben ser identificados y medidos. Respecto de la contaminación del aire, sólo basta con disponer de los sistemas de medición adecuados y de los equipos de expertos en la identificación y medición de todos los gases residuales y fugitivos que el cordón industrial de cada zona impone, para tomar acciones en relación a las nuevas normas de calidad primaria, que efectivamente protejan la salud de las personas y análogamente, en relación a las normas secundarias para proteger la biodiversidad.

Una vez determinadas las concentraciones de los contaminantes deberán compararse con las nuevas normas de calidad para todos los contaminantes encontrados, y se determinarán las prioridades de zonas a descontaminar. Así, se podrán convocar a otros equipos de profesionales expertos en descontaminar todos los lugares que imponen riesgos de salud (los cuales deben estar privados del acceso público).

Una vez efectuada la evaluación de expertos en descontaminación, quienes deben utilizar las más avanzadas técnicas disponibles en el mercado nacional e internacional, se deben planificar las actividades a realizar, identificando los costos de cada una de las etapas, para todos todos los procesos de descontaminación (aire, suelos y aguas).

Posteriormente, se debe definir la fórmula justa de prorratear los costos del plan de descontaminación, entre todas las empresas contaminantes de los cordones industriales de cada localidad y el Estado que les ha permitido contaminar por años y décadas.

Dado el simple análisis de pasos a seguir, mencionado anteriormente, al observar el plan de descontaminación presentado, constatamos que no contiene una secuencia lógica de etapas y procesos o actividades, no define las áreas de instituciones responsables de liderar cada etapa o proceso, tampoco se menciona con qué profesionales externos y equipamiento se llevará a cabo cada etapa, ni los costos asociados por etapa, ni su financiamiento, tampoco, existen plazos a etapas no existentes, ni tratadas de manera global.

Por lo tanto, no existe un plan de descontaminación, donde su eficacia quede demostrada al comparar valores actuales de contaminación, para cada uno de los tóxicos ambientales existentes al día de hoy, en suelos, aguas y aire, de cada localidad y las nuevas normas de calidad ambiental primaria (aún no definidas) y secundaria (aún no definidas) vs el diferencial que se medirá una vez ejecutado el plan de descontaminación de suelo, aguas y aire, en cada localidad.

Hemos constatado que se hace referencia en el plan a que un pequeño número de empresas disminuyan sus normas de emisiones y se entregan procedimientos para minimizar la emisión de más contaminantes al ambiente durante el transporte, para minimizar la acumulación de contaminación en los suelos.

Por lo tanto, lo que se entregado como Plan de Prevención y Descontaminación corresponde a directrices generales para reforzar las normas de operación de las empresas, con un pequeño incapié en que las emisiones de gases al año disminuyan levemente, respecto de lo que las normas establecidas permiten, sin multas por incumplimiento ni penalidades.

Por lo tanto, la palabra Descontaminación no corresponde al contenido del plan. (RAE: Someter a tratamiento lo que está contaminado, a fin de que pierda sus propiedades nocivas).

4.4. Comentarios Finales

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Observaciones:

Deberían planificarse reducciones para cumplir con normas primarias chilenas en un plazo máximo de 3 años, y luego llegar a las normas recomendadas por OMS en los 3 años siguientes. Además agregar y/o homologar normas OMS para otros agentes contaminantes. No obstante, de acuerdo a lo descrito en detalle, aunque se cumplan las normas primarias MP, SO2 y NOx no se soluciona los problemas de toxicidad como los ocurridos entre Agosto y Octubre porque dichos episodios fueron causados por otros agentes no evaluados.

Además la ONEMI debe tener un plan de acción frente a contingencias químicas y no improvisar sin plan alguno.

Las accione propuestas más abajo (vide infra) pueden ser resumidas de la siguiente manera:

RESUMEN DE ACCIONES IMPRESCINDIBLES PARA CONFORMAR UN REAL PLAN DE PREVENCION Y DESCONTAMINACION:

A. PROPOSICIONES PARA EL PLAN DE PREVENCION DE EMERGENCIAS SANITARIAS

1. **ADOPTAR DE NORMAS OMS Y NORMAS BASADAS EN EL PRINCIPIO PRECAUTORIO PARA LO QUE NO ESTE NORMADO**

2. **FISCALIZAR PERMANENTE TODOS LOS CONTAMINANTES EN EL AMBIENTE**

Mediciones de contaminantes alrededor de las empresas

Mediciones de contaminantes en las chimeneas de las empresas

Mediciones de contaminantes en puntos de tránsito o permanencia de personas

Las tendencias históricas de las concentraciones de contaminantes ambientales, positivas o negativas, para la ubicación de los equipos de medición no aplican por las siguientes razones:

Se deben efectuar permanentes análisis de espectro de gases en el ambiente para posicionar, adecuadamente, los equipos de medición.

3. **ACTUALIZAR NORMAS RELATIVAS A CONTAMINANTES PARA PREVENIR EFECTOS EN LA SALUD DE LAS PERSONAS**

4. **DISPONER DE CENTROS DE ASISTENCIA MEDICA SUFICIENTES PARA HACER FRENTE A EMERGENCIAS POR CONTAMINACION MASIVA**

5. **PREVENIR EMERGENCIAS EN TURISTAS QUE DESCONOCEN LA GRAVEDAD DE LA CONTAMINACION EN ESTAS ZONAS**

6. **PREVENIR QUE NUEVOS PROYECTOS IMPONGAN RIESGOS A LA SALUD DE LAS PERSONAS Y REVISAR TODOS LOS PROYECTOS ANTERIORES**

7. **PREVENIR QUE EL PERSONAL OPERACIONAL DE LAS EMPRESAS DESCONOZCA LOS RIESGOS QUE IMPONE A LA POBLACION AL NO CUMPLIR PROCEDIMIENTOS**

8. **PREVENIR AUMENTO DE STRESS POR FALTA DE FUENTE LABORAL PROVOCADA POR LA CONTAMINACION**

9. **PREVENIR QUE LA ONEMI NO POSEA PERSONAL COMPETENTE O PROCEDIMIENTOS ADECUADOS PAREA ENFRENTAR EMERGENCIAS**

10. **PREVENIR NO SE ABANDONE LA ASISTENCIA PERSONAS POR NO CONTAR CON AMBULACIAS SUFICIENTES**

11. **PREVENIR QUE SE INCUMPLAN NORMAS DE SEGURIDAD DE LOS TRABAJADORES**

12. **PREVENIR QUE SE CAMBIEN DIAGNOSTICOS DE PACIENTES PARA OCULTAR GRAVEDAD DE LA SITUACION DE CONTAMINACION**

13. **PREVENIR QUE LAS PERSONAS AFECTADAS CRONICA Y DIRECTAMENTE POR LA CONTAMINACION PERMANEZCAN SIN ATENCIÓN POR FALTA DE RECURSOS**

14. . PREVENIR EL DETERIORO DE LA SALUD DE LA POBLACION DURANTE EMERGENCIAS

14.1 Evacuar a toda la población infantil y mujeres embarazadas de las zonas afectadas cuando se produzcan emergencias sanitarias

14.2 Para eventos de emergencia sanitaria la ONEMI Nacional, debe convocar y coordinar las actividades de las diferentes entidades implicadas en la institucionalidad ambiental y laboral
14.3 Crear un plan de emergencia química en esta zona, para rescate del personal en las plantas industriales y para rescate de la población afectada,

15. PREVENCION DE NUEVOS EPISODIOS DE CONTAMINACION

16. PREVENIR QUE CONTINUEN PROBLEMAS AMBIENTALES CON REPERCUSION EN LA SALUD, POR FALTA DE PROFESIONALES ESPECIALISTAS EN APORTAR SOLUCIONES

B. PROPOSICIONES PARA EL PLAN DE DESCONTAMINACION

1. **PRECISAR EL ALCANCE DE LA DESCONTAMINACION**
2. **DESCONTAMINAR EL MAR, FRUTAS HORTALIZAS Y AGUAS DE RIEGO**
3. **INCORPORAR ENERGIAS RENOVABES NO CONVENCIONALES EN LAS EMPRESAS CONTAMINANTES**
4. **EXPLICITAR FUENTE DE FINANCIAMIENTO DEL PLAN DE DESCONTAMINACION**
5. **PLANIFICAR TODAS LAS ETAPAS DEL PLAN DE DESCONTAMINACIÓN Y RESPONSABLES**

DETALLE DE LAS ACCIONES IMPRESCINDIBLES PROPUESTAS PARA CONFORMAR UN REAL PLAN DE PREVENCION Y DESCONTAMINACION:

A. PROPOSICIONES PARA EL PLAN DE PREVENCION DE EMERGENCIAS SANITARIAS

1. **ADOPTAR DE NORMAS OMS Y NORMAS BASADAS EN EL PRINCIPIO PRECAUTORIO PARA LO QUE NO ESTE NORMADO**

   Validar legalmente, para que tengan efecto jurídico vinculante en Chile, como normas primarias de calidad ambiental, los estándares, normas y parámetros de la OMS, actualmente vigentes en dicha institución, para la totalidad de los

productos, insumos, compuestos, inmisiones, emanaciones, efluentes y descargas al medio ambiente, mediante una homologación directa y vinculante a través de un acto administrativo de parte del Estado de Chile, para dichos parámetros, normas y estándares, de aplicación inmediata para la zona de latencia y/o saturación de Quintero-Puchuncaví y Concón. Ello debe abarcar y aplicar a la totalidad de los productos, insumos, compuestos, inmisiones, emanaciones, efluentes y descargas contaminantes, que emanen o puedan emanar, que se emitan o se puedan emitir, por las actividades antropogénicas en las tres comunas. Ello debe aplicar sin restricciones para normas de calidad del aire, del agua potable y de riego, aguas recreacionales y de usos generales e igualmente para suelos, independientemente, de su calidad, categoría o clasificación.

Para elementos o compuestos no normados por la OMS, se deberán considerar los estudios científicos más restrictivos que existan, para definir los límites máximos de exposición de las personas, bajo el Principio Precautorio, validados por el Ministerio de Salud y el Colegio Médico de Chile, con los especialistas que les competa.

La materialización legal, de lo anteriormente expuesto, se puede concretar en muy breve plazo mediante la dictación de un Decreto Supremo, a partir de la denominada potestad reglamentaria autónoma del Presidente de la República.

2. FISCALIZAR PERMANENTE TODOS LOS CONTAMINANTES EN EL AMBIENTE

Instalación de un número considerado como, técnicamente suficiente, de equipos o estaciones de medición nuevas y de tecnología de punta para la medición de contaminantes ambientales, que no podrá ser inferior a 1000 equipos/estaciones de medición, de última generación, con al menos 30 equipos analizadores de espectro móviles, y todos los equipos específicos que sean para medir todos los gases en las chimeneas de las empresas. Los dos o tres equipos que la SMA, espera disponer para monitoreo de gases para mediciones estáticas en un solo punto, no sirven.

Las mediciones de las estaciones de medición deben efectuarse de manera contínua (datos al seg, min u horas), operados de manera remota, por personal capacitado y sin conflicto de interés (ya sea municipal o dependiente del Ministerio de Salud), o a través de entidades externas, con metodologías auditables y certificables. Debe existir comunicación pública, en línea y continua, de las concentraciones de cada contaminante, en valores absolutos y no de promedios (nombre del compuesto, valores mínimos, máximos y horarios en que se producen las mayores concentraciones), todos medidos durante las 24 horas, entregando información al menos horaria, en cada día calendario.

Mediciones de contaminantes alrededor de las empresas

Todas las empresas deberán tener al menos 4 estaciones de medición de contaminantes a su alrededor, colocados a distintas alturas tal que refleje el peor escenario para la pluma de dispersión de gases regulares y potenciales fugitivos, que con condiciones climáticas desfavorables pueda afectar la salud de las personas. Los equipos de mediciones, la responsabilidad de su operación y fiscalización, manera remota, será de la Superintendencia de Medio Ambiente (SMA) o entidad que ella designe para ello.

Mediciones de contaminantes en las chimeneas de las empresas

Todas las empresas deben inslalar sistemas de medición de gases, con equipos de última generación, en cada una de sus chimeneas, de manera contínua. La fiscalización de manera remota, en tiempo real y con sistemas en línea, debe ser de responsabilidad del Seremi de Medioambiente Regional.

Por lo tanto, las normas máximas de emisiones que, actualmente, son medidas en toneladas al año, deben ser referidas a valores máximos diarios, no sólo para los gases que hoy se miden de manera discreta (PM 2,5, PM 10, SO2, NOx), sino todos los gases que impongan riesgos a la salud, ante escenarios adversos de ventilación.

Mediciones de contaminantes en puntos de tránsito o permanencia de personas

Las estaciones de monitoreo actuales con rango de representatividad de 2 Km, no reflejan lo que sucede en puntos intermedios, pues las edificaciones, árboles, topografía de la zona, contaminación por transporte público y otras fuentes, varían las mediciones, aún cuando las variables climáticas sean similares. Lo que interesa medir es la exposición real de los habitantes, sin condiciones especiales de aislación de factores.

Los equipos o estaciones de medición, deben tener la capacidad para medir todos los gases considerados como tóxicos, según la OMS y/o según los nuevos agentes tóxicos que el MINSAL defina, además del material particulado. Es decir, debe poder identificar y medir todos los componentes tóxicos de productos, insumos, compuestos, inmisiones, descargas, efluentes y emanaciones, que las empresas emiten al ambiene. Además, deben contar con indicadores específicos de representatividad poblacional (jardines infantiles, colegios, hospitales, parques, calles o sectores más concurridos).

Las tendencias históricas de las concentraciones de contaminantes ambientales, positivas o negativas, para la ubicación de los equipos de medición no aplican por las siguientes razones:

a. No haberse medido las emanaciones de todos los gases causantes de las emergencias de manera contínua y permanentemente, en el pasado.
b. Dado el creciente parque industrial de la zona que genera la saturación por múltiples contaminantes (muchos de ellos no normados y sin historia)

IMPORTANTE

Se deben efectuar permanentes análisis de espectro de gases en el ambiente para posicionar, adecuadamente, los equipos de medición. Pues deben estudiarse y considerarse los horarios de mayor probabilidad de obtener valores más altos, tanto en los equipos de representación poblacional como en los que se ubicarán en los bordes de las empresas, para ver si es necesario un reposicionamiento.

3. ACTUALIZAR NORMAS RELATIVAS A CONTAMINANTES PARA PREVENIR EFECTOS EN LA SALUD DE LAS PERSONAS

Eliminar las condiciones de superación y metodologías que no tienen sentido para proteger la salud de la población, para diversas normas de contaminantes ambientales.

Aquí se indica un ejemplo, de una norma vigente:

PARA MATERIAL PARTICULADO FINO RESPIRABLE MP 2,5

a) Cuando el percentil 98 de los promedios diarios registrados durante un año, sea mayor a 50(µg/m3), en cualquier estación monitora calificada como EMRP; o
b) Cuando el promedio tri-anual de las concentraciones anuales sea mayor a 20(µg/m3), en cualquier estación monitora calificada como EMRP.

Si el periodo de medición en una estación monitora no comenzare el 1º de Enero, se considerarán los tres primeros periodos de 12 meses a partir del mes de inicio de las mediciones, hasta disponer de tres años calendario sucesivos de mediciones.

Si al cabo de un año, en alguna de las estaciones de monitoreo de calidad del aire clasificadas como EMRP, se verifica la superación de la presente norma, su frecuencia de medición deberá ser diaria.

Basta con que se superen las normas definidas por la OMS y/o los límites máximos que el MINSAL defina, para que la Seremi de Medio Ambiente Regional ordene detener, de inmediato, las operaciones de las empresas cuyas concentraciones de sus gases infrinjan las normas. Esto implica que la vigilancia de la SMA Regional debe ser continua durante el día y la noche, utilizando los sistemas de monitoreo en línea. Así, deberá tomar la decisión de aplicar los planes de pre emergencia o emergencia, llegando eventualmente, a suspender las operaciones de las empresa que contribuyan con esas emisiones, incluso en horario nocturno.

4. DISPONER DE CENTROS DE ASISTENCIA MEDICA SUFICIENTES PARA HACER FRENTE A EMERGENCIAS POR CONTAMINACION MASIVA

Instalar un Consultorio de Salud para cada localidad, especializado en Contaminación Ambiental, con medios materiales, recursos humanos y tecnológicos, equipos, instrumentales y personal calificado y capacitado para enfrentar emergencias sanitarias de tipo industrial. Además, se requiere definir una metodología científica para la atención adecuada de la población que ha sido expuesta durante decenios a tóxicos dañinos para la salud.

5. PREVENIR EMERGENCIAS EN TURISTAS QUE DESCONOCEN LA GRAVEDAD DE LA CONTAMINACION EN ESTAS ZONAS

No reactivar el turismo en Quintero, Puchuncaví y Concón, por ser zonas altamente contaminadas. Sino todo lo contrario, se debe advertir de manera escrita a los turistas, en todos los pasos fronterizos del país, evitar ir a estas zonas, por las sucesivas alerta ambientales que afectarán a personas sensibles. No se puede exponer a turistas a que visiten una zona hasta que se encuentre descontaminada.

6. PREVENIR QUE NUEVOS PROYECTOS IMPONGAN RIESGOS A LA SALUD DE LAS PERSONAS Y REVISAR TODOS LOS PROYECTOS ANTERIORES

Elaborar una Guía de Evaluación de Impacto Ambiental de Inmisiones, Emanaciones, Efluentes y Descargas (IEED) de Plantas Químicas, Industriales y Similares, para establecer criterios de evaluación para los órganos de la

administración del Estado con competencia ambiental. En ella se debe asegurar que dentro de los factores críticos de decisión, respecto de las Comunidades Sociales, se incorporen los efectos en la salud por las IEED, que en concentraciones determinadas o que en conjunto con otros contaminantes (aunque estén dentro de la norma), produzcan sintomatologías que deterioren la salud de la población.

Un ejemplo para emanaciones de gases tóxicos sería si por efecto del uso de leña o ante humo de incendios o alta contaminación por PM 2,5, además existieran gases muy tóxicos que en pequeñas cantidades generan emergencias de salud en personas sensibles (infantes, niños, adultos mayores o cualquier persona con alguna enfermedad cardiovascular o pulmonar o respiratoria u otras en que le generen deterioros de salud). En este caso, se debe obligar a todos los actores contaminantes que disminuyan, de inmediato, sus emanaciones. Para ello, hay que analizar cuales son los gases contaminantes críticos de las empresas del cordón, que en combinación con otros gases, generan los cuadros de salud.

Se puede constatar que los efectos en la salud descritos en estudios científicos, analizado para un solo componente tóxico, es mucho más grave para la realidad diaria de contaminación ambiental que sufre cada localidad, donde el deterioro de salud a mediano y largo plazo, es fácilmente demostrable.

Por lo tanto, la Autoridad debe asimilar que los factores de precupación de las comunidades y en particular las personas expuestas a agentes tóxicos, ordenados por prioridad, son los siguientes:

1. Deterioro de salud
2. Deterioro de su cadena alimentaria
3. Deterioro de su fuente laboral y/o su imposibilidad cumplir con su trabajo (por problemas de salud)
4. Deterioro financiero producto de la baja en la economía de la región (causada por la contaminación)
5. Deterioro del paisaje
6. Deterioro del patrimonio cultural.

Por lo tanto, si actualmente faltan los primeros cuatro puntos, en los factores de críticos de decisión en la Evaluación Ambiental Estratégica, ellos deben ser considerados. Pues, están mucho antes en la escala de valores de las personas para este tipo de amenazas (químicas) a su hábitat, que los que actualmente se están usando (sólo los puntos 5 y 6.).

Los primeros dos puntos, son en escencia los más críticos de todos, por lo que desde ya deben estar considerados como línea base para el nuevo PPDA. Sino, nada de lo que se haga respecto de los puntos 5 y 6 tendrá sentido, pues la salud de las personas está siendo deteriorada y eso es lo que hay que solucionar, sin alterar su prioridad.

El mismo análisis, se debe realizar para proteger a la biodiversidad, pues falta incluir una serie de factores críticos de decisión, pero ese tema lo dejamos para los especialistas de esas áreas.

7. PREVENIR QUE EL PERSONAL OPERACIONAL DE LAS EMPRESAS DESCONOZCA LOS RIESGOS QUE IMPONE A LA POBLACION AL NO CUMPLIR PROCEDIMIENTOS

Crear una Academia con personal especializado, para capacitar a todos los supervisores operacionales de las empresas del cordón industrial , respecto de sus responsabilidades y operaciones para minimizar o evitar los riesgos inherentes a la manipulación de estanques y otros aspectos, relacionados con una emergencia química. Uno de los objetivos del curso debe ser la minimización de las recurrentes infracciones generadas por las fiscalizaciones del Seremi de Medio Ambiente, en sus plantas.

8. PREVENIR AUMENTO DE STRESS POR FALTA DE FUENTE LABORAL PROVOCADA POR LA CONTAMINACION

Planificar la forma de transferir nuevos conocimientos a las personas afectadas en sus trabajos por la contaminación, para mantenerlos productivos, evitando generar situaciones de mayor stress ante pérdidas de puestos de trabajo por áreas contaminadas.

La economía regional ha sufrido y sigue sufriendo pérdidas que son de presunta responsabilidad del Estado de Chile y las empresas que por décadas han contribuido a ello al igual que las que últimamente, se han incorporado o diversificado sus operaciones, afectando aún más el ambiente.

9. PREVENIR QUE LA ONEMI NO POSEA PERSONAL COMPETENTE O PROCEDIMIENTOS ADECUADOS PAREA ENFRENTAR EMERGENCIAS

Crear un plan de emergencia química en cada localidad, con personal especializado y entrenado para actuar en la primera línea de acción, para el rescate del personal en las plantas industriales y para rescate de la población afectada, coordinando con los hospitales de la zona y de otros lugares la eficiente atención a los pacientes, probado con simulacros (Plan Daisy).

Se requiere de personal, con indumentaria de protección de punta, que sea capaz de identificar todos los gases tóxicos en las zonas de mayor impacto, de manera inmediata, con equipos y metodologías apropiadas, evitando los vacíos que han existido al respecto hasta el día de hoy. Las mediciones de gases realizadas por especialistas en emergencias químicas, deben ser independientes a las mediciones de gases provenientes de los sistemas de mediciones que la autoridad entregue. La razón es que, simplemente, sus equipos pueden estar mal ubicados y no reflejar la situación real de contaminación de la pluma de dispersión de gases tóxicos.

Es necesario distinguir que las responsabilidades del Comité de Emergencia (COE) locales definidas para enfrentar la emergencia, son muy diferentes al personal de asistencia directa relacionada con la salud. Pues, ellos no son técnicos especialistas en las labores indicadas anteriormente. Por lo tanto, no se podría aceptar que alguno de ellos o sus dependientes, pudieran operar aparatos de medición de gases, que obedecen a una metodología creada por especialistas en emergencias químicas, menos aún si no disponen de los equipos de protección adecuados *(que no se vea una nube de gases no significa estar a salvo*). El no contar con la información de los gases a los que una persona ha estado expuesta, al momento de su atención médica, puede ocasionar serios riesgos para su salud, como mostró en el informe del Colegio Médico, ya entregado.

10. PREVENIR NO SE ABANDONE LA ASISTENCIA PERSONAS POR NO CONTAR CON AMBULACIAS SUFICIENTES

Asignar fondos para la compra no sólo de una ambulancia para Quintero, sino tres al menos, para los centros de atención en cada una de las zonas contaminadas (Quintero, Concón y Puchuncaví), dadas las recurrentes emergencias que afectan del orden de 50 a 100 personas a la vez.

11. PREVENIR QUE SE INCUMPLAN NORMAS DE SEGURIDAD DE LOS TRABAJADORES

Los trabajadores que laboran en procesos que generen emisiones tóxicas, en cualquiera de las fases en que se haya originado la emergencia al ambiente, deberían estar bajo programas de vigilancia epidemiológica ocupacional. Los

organismos Administradores del Seguro Ley 16.744 deben proporcionar los servicios de asesoría y vigilancia para esas empresas. Los organismos fiscalizadores, SEREMI de Salud y Dirección del Trabajo, deben estar efectuar las inspecciones y tomar las medidas, inmediatas, según la peligrosidad lo amerite, incluida la suspensión de faenas. El laboratorio nacional de referencia (Instituto de Salud Pública) debe prestar los servicios requeridos para el análisis de muestras ambientales y de las personas expuestas, así como asegurando que los laboratorios, públicos o privados, que presten dichos servicios, cumplan con estándares de calidad.

12. PREVENIR QUE SE CAMBIEN DIAGNOSTICOS DE PACIENTES PARA OCULTAR GRAVEDAD DE LA SITUACION DE CONTAMINACION

Eliminar la medida adoptada donde los pacientes policonsultantes (tres consultas o más) sean derivados a Salud Mental. La Mesa Regional de Salud Mental, activó los equipos de Apoyo de Respuesta de Salud Mental (Arsam), desplegados en la zona afectada, para trabajar en conjunto con el equipo del Hospital de Quintero al respecto, según el Informe de Gestión Quintero-Puchuncaví, del 20 de Septiembre, 2018.

Esta medida agravará los cuadros de salud al dejarlos sin la atención que corresponde. Es más lógico que esos pacientes sean vistos por neurólogos, que podrían constatar que el cuadro presentado es típico de gases que afectan el sistema nervioso, o sean vistos por otros profesionales médicos especializados en intoxicaciones (de ACHS, por ejemplo, si no dispusiera de un especialista de turno, en el momento de la atención).

No se puede aceptar que se instituya el cambio de diagnóstico de los pacientes con síntomas recurrentes causados por la contaminación ambiental de las zonas afectadas. Esto constituye un hecho grave y al Colmed le compete investigar, cada uno de los casos que se hayan enviado al Salud Mental, durante el período completo desde que se inició la primera emergencia de salud.

Todos los centros de atención deben reflejar los síntomas y diagnósticos médicos, por cada vez que el paciente concurra. El no escuchar y atender al paciente que vive bajo una permanente nube de contaminantes tóxicos, aún no identificados ni medidos, es un hecho grave. Por lo tanto, el paciente no puede ser desatendido en el mérito de su cuadro de salud, potencialmente relacionado con la contaminación ambiental de la zona.

13. PREVENIR QUE LAS PERSONAS AFECTADAS CRONICA Y DIRECTAMENTE POR LA CONTAMINACION PERMANEZCAN SIN ATENCIÓN POR FALTA DE RECURSOS

Asegurar, de por vida, la futura atención en salud de todos los habitantes de las Comunas de Quintero y Puchuncaví, por secuelas al haber sido expuestos crónicamente (cáncer) y/o perinatalmente a los diversos contaminantes del parque industrial actual, dictando una ley similar a la aprobada para los efectos a mediano y largo plazo de los polimetales en Arica.

14. PREVENIR EL DETERIORO DE LA SALUD DE LA POBLACION DURANTE EMERGENCIAS

14.1 Evacuar a toda la población infantil y mujeres embarazadas de las zonas afectadas cuando se produzcan emergencias sanitarias definidas de acuerdo a orientaciones internacionales. Se debe prevenir el riesgo inminente de mujeres embarazadas y menores de 2 años por los daños irreversibles casados por el mecanismo de imprinting epigenético, descrito en informes anteriores. Esta evacuación deberá ser voluntaria, pero debe proveerse del transporte y alojamiento necesarios. También, es necesario CONSIDERAR LA SITUACIÓN DE GRUPOS VULNERABLES: enfermos del sistema cardiovascular y/o respiratorio, crónicos, enfermos agudos, con medicamentos que exaserven efectos secundarios y a las personas más sensibles en general.

14.2 Para eventos de emergencia sanitaria la ONEMI Nacional, debe convocar y coordinar las actividades de las diferentes entidades implicadas en la institucionalidad ambiental y laboral, que están llamadas a cumplir su rol en la prevención de emergencias de este tipo. Incluyendo en ésto a los organismos relacionados con la prevención de riesgos industriales y organismos fiscalizadores, que de otras regiones deban estar presentes en la zona afectada, al más breve plazo. La ONEMI a nivel nacional debe tomar en consideración la opinión y reclamos de la comunidad afectada, en la toma de decisiones y transparentar las acciones para manejar la crisis. La ONEMI Regional deberá solicitar a la ONEMI Nacional contar con los profesionales técnicos y equipos de mediciones necesarios, en los tiempos mínimos que se requieren, para determinar los agentes tóxicos que causan la emergencia, para que los profesionales de salud puedan atender a los pacientes, adecuadamente.

14.3 Crear un plan de emergencia química en esta zona, para rescate del personal en las plantas industriales y para rescate de la población afectada, coordinando con los hospitales de la zona y de otros lugares la eficiente atención a los pacientes, probado con simulacros (Plan Daisy).

15. **PREVENCION DE NUEVOS EPISODIOS DE CONTAMINACION**

15.1 Suspender y/o condicionar el funcionamiento de empresas con permisos industriales ya otorgados, supeditados al cumplimiento de las nuevas normas homologadas (OMS) con validez legal en Chile.

15.2. Paralizar, inmediatamente, nuevos permisos a nuevas fuentes que contribuyan a empeorar la actual situación de saturación de emisiones, en la V región.

15.3 Actualización toxicológica de toda la población expuesta, con delimitación y clausura de los lugares contaminados y su prohibición de uso para todo fin, hasta la descontaminación total del suelo e instalaciones.

16. PREVENIR QUE CONTINUEN PROBLEMAS AMBIENTALES CON REPERCUSION EN LA SALUD, POR FALTA DE PROFESIONALES ESPECIALISTAS EN APORTAR SOLUCIONES

En Chile, existen excelentes centro de investigación, en prestigiosas universidades a través de las cuales la Institucionalidad de Salud y Medio Ambiente, puede solicitar asesoría. Ellos, conocen muy de cerca los problemas ambientales de la zona y pueden generar excelentes recomendaciones dada su integración multidisciplinaria para resolver problemas complejos. Asímismo, los diversos Colegios y Sociedades Profesionales, empresas consultoras nacionales e internacionales, pueden asistir con asesorías para proyectos específicos que se requieran resolver.
Sin desmerecer el aporte de la OMS y OPS, ellos poseen a este respecto una mirada mucho más global de lo que la problemática en sí engendra. Esto significa que en base a los reportes que estas organizaciones emitan, los centros especializados pueden profundizar mucho más los aspectos críticos a ser resueltos y el camino hacia una solución integral será más rápida, por la vía de los espacialistas nacionales o con participación conjunta internacional.
Desde ya el Colegio Médico de Chile, ofrece su capacidad para realizar algún tipo de asesoría que se requiera, en el ámbito de sus competencias o integrar comisiones multidisciplinarias, cuando se solicite.

B. PROPOSICIONES PARA EL PLAN DE DESCONTAMINACION

1. PRECISAR EL ALCANCE DE LA DESCONTAMINACION

Abarcar no sólo el material particulado PM10, PM 2,5, Dióxido de Azufre, y otros actualmente, monitoreados. Sino también, medir y monitorear el particulado PM ultrafino < de 2,5, Mercurio, Plomo, Cadmio, Manganeso, Cromo y todos los que se encuentren dañando el ambiente. Además, se debe realizar la más estricta monitorización, normativa y regulación de los todos los Compuestos Orgánicos Volátiles, así como de otros componentes de alta toxicidad constituyentes de los particulados, como el Arsénico, que sigue sin norma ni regulación desde 1994. Es decir, se deben descontaminar todos los compuestos y elementos tóxicos emanados del cordón industrial, para proteger la

salud de las personas y la biodiversidad, sean emitidos en el presente o en el pasado, causando el daños al ambiente y a los ecosistemas, de cada localidad.

2. DESCONTAMINAR EL MAR, FRUTAS HORTALIZAS Y AGUAS DE RIEGO

2.1 Solicitar mediciones de metales pesados en mariscos, peces, flora y fauna marina, a las entidades correspondientes, dado que ya se han realizado estudios donde se concluye que están fuera de las normas de la UE y FAO. Adicionalmente, se requieren mediciones de metales pesados en frutas y hortalizas y sus aguas de riego.

2.2 Incentivar la desintoxicación natural de las aguas marinas (algas). Entregar avances y resultados del Proyecto de Bioremediación para la Bahía de Quintero, impulsado por Ministerio de Medio Ambiente, que comenzó en el 2014 y está proyectado para 12 años.

2.3 Informar, públicamente los avances de manera paralela y complementaria al PRAS (Programa para la recuperación ambiental y social) de Quintero, Puchuncaví y Concón, de manera períodica.

Todos los avances del plan de descontaminación debe estar publicado en un sitio web, que muestre claramente los avances y los atrasos de todas las etapas de cada proyecto. Además, se debe alertar respecto de todas las zonas donde se haya afectado la cadena alimentaria.

3. INCORPORAR ENERGIAS RENOVABES NO CONVENCIONALES EN LAS EMPRESAS CONTAMINANTES

Acelerar la reconversión de todas las industrias y las plantas a energías eléctricas no contaminantes[3], dando de baja y reemplazando actuales fuentes de contaminación obsoletas por ERNC[4], estipulando una fecha máxima para cumplir con esta reconversión, sino aplicar sanciones drásticas por incumplimiento.

4. EXPLICITAR FUENTE DE FINANCIAMIENTO DEL PLAN DE DESCONTAMINACION

La descontaminación del suelo, aire y aguas de las zonas contaminadas, debe ser bajo los nuevos estándares, normas y parámetros normativos de exigencias reglamentarias sanitarias y ambientales con validez legal. Este proyecto de

[3] Del mismo modo como lo están haciendo en sus países de origen (Ej. AES Gener)

[4] y adecuar la Planta ENAMI Ventanas a estándares internacionales en cuanto a procedimientos.

descontaminación sanitario - ambiental deberá ser financiado, en partes iguales, entre todas las empresas del complejo industrial de cada localidad y el Estado que las ha autorizado a operar.

5. PLANIFICAR TODAS LAS ETAPAS DEL PLAN DE DESCONTAMINACIÓN Y RESPONSABLES

Planificar en detalle cómo, quiénes y cuándo se efectuarán los procesos de descontaminación. Para luego, corroborar con mediciones in situ las concentraciones de cada contaminante y puedan estar disponibles para su uso y cuidado, si cumplen con las nuevas normas de calidad primarias y secundarias.

ADDENDUM AL INFORME ANTERIOR

Adicionalmente, a todos los efectos de salud que el Colegio Médico presentó para ser considerado como antecedente en la elaboración del PPDA Q-P-C, se presenta un nuevo estudio:

EFECTOS DEL MATERIAL PARTICULADO SOBRE LA SALUD

Diabetes Mellitus

Se ha postulado, recientemente, en el estudio con más casuística en el tema, que la exposición prolongada a PM1, PM2,5 y PM10 se asocia a la aparición de Diabetes tipo 2, especialmente, en individuos menores de 50 años y con sobrepeso. Hay bases de datos con meta-análisis de 17 estudios que han encontrado asociación significativa entre Diabetes tipo 2 y 6 contaminantes aéreos (PM10, PM2·5, dioxido de nitrógeno [NO2], ozono [O3], sulfatos, y dióxido de azufre [SO2]), con risk ratios y risk ratios de mortalidad en rangos de aumentos de 1·01/10 µg/m3 a 1·07/10 µg/m3 en tales elementos. Otro meta-análisis incluyó 13 estudios originados en Norte America y Europa, que reportan que el riesgo de Diabetes Tipo 2 aumenta en un 10% por cada 10 µg/m3 de aumento del PM2·5 y en un 8% por cada 10 µg/m3 de NO2. (Angel M Dzhambov, 2018).

Propuestas de Comisión Lancet

Propuestas de Comisión Lancet (Revista Lancet, 19 Octubre de 2017) respecto a cómo enfrentar el problema de la contaminación y su relación con la salud.

Las propuestas a continuación detallan una hoja de ruta a considerar cuando se enfrenta internacionalmente, con seriedad y determinación el problema, dadas las enormes implicancias humanas y económicas que abarca:

I. Explorar vínculos causales entre contaminación, enfermedad y daño subclínico, por ejemplo entre niveles de contaminación del aire y alteraciones del SNC en niños y ancianos;
II. Cuantificar la carga global de enfermedad asociada a contaminantes químicos de reconocida toxicidad, tales como plomo, mercurio, cromo, arsénico, asbesto e hidrocarburos;
III. Identificar y caracterizar los resultados de salud adversos causados por contaminantes químicos nuevos y emergentes, tales como neurotóxicos, disruptores endocrinos, nuevos insecticidas, herbicidas químicos y desechos farmacéuticos;
IV. Identificar y mapear los riesgos de contaminación especialmente en las zonas y/o países de ingresos bajos y medianos;
V. Mejorar las estimaciones de los costos económicos de la contaminación y las enfermedades relacionadas con la contaminación;
VI. Y medir los beneficios de las intervenciones contra la contaminación sobre la salud y la economía versus los costos de las intervenciones.

Referencia Bibliográfica

Dzhambov, Angel. Ambient Air Pollution and diabetes in China. The Lancet Planetary Health, Volume 2, Issue 2, February 2018, Pages e52-e53. Informe Comisión Lancet: http://crossmark.crossref.org/dialog/?doi=10.1016/S0140-6736(17)32345-0&domain=pdf

4.5. Anexos

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Depto M.A. Colegio Médico de Chile
Observaciones:

ANEXO

El PPDA presentado posee objetivos muy distintos a lo esperado, para evitar episodios de contaminación que imponen riesgos de salud en las personas. El PPDA en su esencia es una recomendación para un grupo de tres empresas, para bajar sus emisiones de PM, SO2 y NOx, sin que las permisivas normas vigentes asociadas sean modificadas, y se define que estas disminuciones comiencen a regir al tercer año de el año siguiente de entrar en vigencia el plan.

El plan contempla algunas buenas normas generales, para limitar la contaminación generada por acopios y otros, pero sin que se definan expresamente el tipo de fiscalización a los procedimientos de confinación y traslado de ese tipo de fuentes contaminantes, ni las multas asociadas para quienes no cumplan con lo que se define en PPDA.

Observamos que varios temas han quedado fuera del PPDA y que la propuesta definida no logrará el objetivo de prevenir nuevos episodios de contaminación, dadas estas omisiones, falencias e incongruencias constatadas.
A continuación se señalan y analizan, sólo algunas de ellas:

1. Objetivo del PPDA es incongruente con el objetivo global de prevenir episodios de contaminación con efectos en la salud, por efectos de diversos gases. Si son PM 2,5 o PM 10, es irrelevante, pues interesa la identificación y concentración de todos los gases, potencialmente tóxicos. Además, el plazo no corresponde a la necesidad inmediata.

> Artículo 1. El presente Plan de Prevención y Descontaminación, en adelante el Plan, regirá en las comunas de Concón, Quintero y Puchuncaví, y tiene como objetivo evitar la superación de la norma primaria de calidad ambiental para material particulado respirable MP10, como concentración anual, y de la norma primaria de calidad ambiental para material particulado fino respirable MP2,5, como concentración de 24 horas, y recuperar los niveles señalados en la última norma mencionada, como concentración anual, en un plazo de 5 años.

2. Los límites de calidad primaria para PM2,5 y PM10 a los que se hace referencia, no son los límites de la OMS, por lo tanto no existe una protección a la salud. Además, un contaminante que cumpla la norma no asegura que no sea tóxico, por lo que se requiere de su identificación y concentración. No se puede esperar 5 años a que disminuya al nivel deseado. Pretender que no se superen los niveles de latencia, significa estar muy por sobre las recomendaciones de la OMS y el cumplir con bajar los niveles, no significa descontaminar sino contaminar menos.

> La meta del Plan es cumplir la norma de calidad para MP2,5 en su concentración anual y diaria, y la norma de MP10 en su concentración anual, asegurando la descontaminación de la zona y que nunca se superen en ésta los niveles de latencia.
>
> Para esto se establece el congelamiento inmediato de emisiones de las fuentes de emisiones de dióxido de azufre (SO2), óxidos de nitrógeno (NOx) y compuestos orgánicos volátiles (COVs), y de su disminución progresiva hasta alcanzar la meta total, al quinto año. Esta medida se justifica por el aporte que tienen estas emisiones en la formación de aerosoles secundarios, que inciden directamente en la formación del material particulado MP2,5.

3. El PPDA no define cambios en los límites de emisiones de las normas actuales (ton/año), tal que se asegure cumplir con las normas de calidad primarias de la OMS (en ug/m3) suguientes:

MP2,5: 10 µg/m3, media anual
25 µg/m3, media de 24 horas

MP10: 20 µg/m3, media anual
50 µg/m3, media de 24 horas

Sino que, vagamente, se define que deben disminuir las emisiones PM2,5 cada año y disminuir las concentraciones de PM10 y PM2,5 de tres años. Lo cual es incoherente con la necesidad de disponer de las concentraciones diariamente, para comprarlas con las normas OMS y tomar medidas para bajar la contaminación si son sobrepasadas.

1. Disminución de las concentraciones diarias máximas de MP2,5, percentil 98, para cada año.
2. Disminución de las concentraciones trianuales de MP10 y MP2,5.

4. No se puede concluir que porque existe un promedio de 3 años más bajo, no han existido un sin número de episodio críticos para la salud. Por lo tanto, los promedios incluso diarios, no garantizan que los gases tóxicos en cantidades pequeñas no estén causando efectos nocivos en la población. Se demuestra complacencia son indicadores que no reflejan la realidad.

Las mediciones efectuadas en dichas estaciones monitoras de calidad del aire, validadas por la Superintendencia del Medio Ambiente desde el año 2012 al 2017, permiten concluir que las concentraciones de MP2,5 han evolucionado positivamente, alcanzando su nivel más bajo en el periodo trianual 2015-2017. Por su parte, la calidad del aire para material particulado respirable MP10 como concentración trianual, se ha mantenido estable durante todo el periodo.

5. No se identifican al resto de empresas y su porcentaje de participación en la contaminación respecto de una serie de compuestos distintos al material particulado, dióxido de azufre y óxidos de nitrógeno, sólo se identifican a tres empresas en la incidencia de estos contaminantes.

Como consecuencia del análisis de la información antes expuesta, se concluye que las mayores fuentes emisoras de la zona corresponden a ENAP Refinerías Aconcagua, AES GENER y CODELCO División Ventanas, por lo cual se establecen metas de reducción de emisiones específicas para cada una de ellas en el presente decreto.

6. La reducción de emisiones para los contaminantes regulados (MP, SO2 y NOx) requerida por el plan se traduce en reducción en concentración **anual de MP2,5 a 4 años plazo, sólo para las grandes fuentes.**

Para la evaluación mencionada se consideraron las medidas de reducción de emisiones para las grandes fuentes, AES GENER, CODELCO Ventanas y ENAP; así como la prohibición de quemas agrícolas y límite de emisión a calderas existentes. La reducción de emisiones para los contaminantes regulados (MP, SO2 y NOx) requerida por el plan se traduce en reducción en concentración anual de MP2,5. Estos resultados se muestran en la siguiente

tabla e indican que casi todos los sectores aportan en cierta medida a la reducción de emisiones, pero que la mayoría de las reducciones se atribuyen a AES GENER, CODELCO Ventanas y ENAP. La reducción de concentraciones debido a la implementación del Plan es progresiva, alcanzando a 1,54 ug/m3 de concentración de MP2,5 para el año 2022, lo que se representa mediante el símbolo Δ.

7. Metodológicamente la forma de analizar los datos provenientes del monitoreo de las empresas, es inadecuado. Cada localidad, presenta realidades diferentes, respecto a sus correspondientes cordones industriales. No se pueden presentar gráficos donde se sumen y promedien las contribuciones de todos, para realizar análisis de la situación global y promediada **a lo largo de tres años**. Esto no conduce a discriminar qué empresas en qué zona son las que contribuyen más a la contaminación ambiental por en algunos tipos de contaminantes.
Por lo tanto, a representación gráfica de la Figura 5 carece de sentido, dado que para el PM 2,5 y el PM 10 se deben tomar acciones de disminuirlos, según los objetivos enunciados. Al separar el PM 2,5 pueden salir otras empresas, no mencionadas, con mayores porcentajes de contribución en la contaminacaión que quedan ocultas al compilar de otra forma los datos para conformar el PM.

8. Casos evitados de mortalidad, en tabla con título equivocado, pues se incluyen otros aspectos.

9. **La disminición de visitas a salas de emergencia** en las tres comunas se menciona que serían **sólo 595 personas**. Si en sólo en 4 o 5 días de episodios de emergencia sanitaria sólo en Quintero y Puchuncaví hubo más de 1000 personas, significa que es imperante incluir nuevas normas para los contaminantes no normados, no conteplados en el presente plan.

Dado, lo anterior, se puede concluir que las emisiones máximas de contaminantes emitidos al ambiente por cada una de esas empresas, anualmente, no es un factor relevante, cuando se desea proteger la salud de las personas. Las normas de calidad primarias y secundarias con limeites de 24 hrs, son los inidcadores críticos que deben ser definidos, de manera complementaria, para avanzar en la definición de un plan de prevención de riesgos de salud.

10. Los reportes de las empresas respecto de sus emeisiones en toneladas al año de contaminantes **no generan acciones de corto plazo** para la protección de la salud de las comunidades. Pues son sólo son número referenciales sin **fiscalización para corroborarlos** y aunque así fuera, estaríamos tardes en un año o tres años para tomar medidas de hechos que ocurrieron en el pasado. Todas las mediciones discretas definidas para que las empresas se autocontrolen, y con posterioridad envíen esos datos no tienen sentido para ejercer una fiszalización, permanente, con el fin de evitar episodios de contaminación con efectos en la salud. Las empresas deben instalar los más avanzados dispositivos de medición en **todos los puntos de emisión de gases residuales y donde exista mayor probabilidad de emisión de gases fugitivos**. Estas mediciones contínuas, deben ser monitoreadas en

línea, de manera permanente por el personal de la SMA. De esta forma las empresas no tendrán que confeccionar informes para conocer sus inventarios de gases, pues todos ellos serán monitoreados de forma remota, al igual que las múltiples (cientos) nuevas estaciones de monitoreo con repersentación poblacional que se deben instalar para disponer de una efectiva fiscalización de todas las empresas, al instante.

11. La forma de cuidar y monitorear que el ambiente apto para permitir la vida sin riesgos de salud, es contar con un número muy grande estaciones de monitoreo con representatividad poblacional, con capacidad para medir todos los agentes contaminantes emanados de los cordones industriales y contar con nuevas normas de calidad primaria, para poder discriminar rápidamente de donde provienen las fuentes de emisión y poder tomar medidas correctivas. Estos aspectos han sido omitidos en el PPDA.

12. Se han omitido los nuevos procedimientos que la ONEMI Regional y Nacional deben tener para hacer frente a emergencias sanitarias como las que se han presentado, para estar a la altura de las circunstacias, convocando al personal especalizado para determinar los gases específicos en el ambiente, que hasta el día de hoy desconocemos.

13. No se puede aceptar que nuevas normas y procedimientos se apliquen a **subconjuntos** de calderas y con desfase para su vigencia, según se plantea:

> Caldera existente: Aquella caldera que se encuentre registrada ante la SEREMI de Salud de acuerdo al D.S. N°10, de 2012, del Ministerio de Salud, hasta cumplido un año desde la publicación del presente decreto.
> Caldera nueva: Aquella caldera que se encuentre registrada ante la SEREMI de Salud de acuerdo al D.S. N°10, de 2012, del Ministerio de Salud, a partir del día siguiente de cumplido un año de la publicación del presente decreto.

Debería decir:

> Calderas existentes son todas las que se encuentren registradas ante la SEREMI de Salud a la fecha de publicación del presente Decreto.
> Calderas nuevas son todas aquellas a ser registradas ante la SEREMI de Salud, luego de la publicación del presente decreto.

14. Una vez instalado el instrumental de medición continua en todos los puntos de emisión (sean calderas nuevas o existentes) cuyos datos deben estar en línea para que la eficiente fiscalización de la SMA a través de sus reparticiones. Será de responsabilidad de la SMA en conjunto con el MINSAL, generar las alertas de contaminación para la ONEMI, cumpla sus funciones. Eliminándose cálculos intermedios, pues interesa conocer la contaminación diaria, no anual, pues es incoherente con el objetivo de prevenir afectar la salud de las personas. Además, la puesta en marcha de estos nuevos sistemas no puede tardar un año a contar de la publicación. Tampoco, hay que crear catastros de calderas afectas o no, pues todas deben cumplir con nuevas normas más restrictivas en beneficios de evitar daños a la salud.

Artículo 6. Las calderas nuevas y existentes, de potencia menor a 20 MWt y mayor o igual a 10 MWt, deberán disponer de instrumentación industrial y/o adecuación necesaria para cuantificar variables que permitan estimar sus emisiones anuales. Las variables a considerar, entre otras posibles, son: (i) consumo de combustible, (ii) caudal, (iii) horas de operación mensual y (iv) otras que permitan estimar adecuadamente el nivel de actividad de las fuentes y sus emisiones, que definirá la Superintendencia del Medio Ambiente, en un plazo de 6 meses contados desde la publicación del presente decreto en el Diario Oficial, mediante los correspondientes protocolos. Esta instrumentación deberá acreditar el monitoreo continuo de esta información y su registro en línea con los sistemas de información de la Superintendencia del Medio Ambiente. Los titulares de calderas existentes dispondrán de un plazo de 12 meses para dar cumplimiento a esta exigencia a contar de la entrada en vigencia de los protocolos dictados por la Superintendencia del Medio Ambiente.

Artículo 7. Para acreditar el cumplimiento de los límites máximos de emisiones de MP, NOx y SO2 establecidos en el artículo 4, las calderas de potencia térmica mayor o igual a 20 MWt, deberán implementar un sistema de monitoreo continuo desde su puesta en operación. Tratándose de calderas existentes, el plazo para la implementación y validación de este sistema, será de 12 meses a contar de la entrada en vigencia de los protocolos dictados por la Superintendencia del Medio Ambiente.

Artículo 8. Con el objeto de tener un catastro actualizado de calderas afectas, en un plazo de 3 meses contados desde la publicación del decreto que aprueba el Plan en el Diario Oficial, todos los titulares de establecimientos que cuenten con calderas de potencia mayor a 300 kWt en el territorio de la zona saturada y latente, deberán enviar una carta a la Superintendencia del Medio Ambiente, declarando el o los tipos de calderas con los que cuentan. En un plazo de 6 meses, la SEREMI de Salud también remitirá a la Superintendencia del Medio Ambiente, el catastro de calderas a su cargo. Dicha declaración deberá incluir: N° de calderas, identificación de cada caldera, potencia térmica en KWt o MWt, tipo de combustible, horas de operación anual en los últimos dos años por cada combustible, emisiones de MP, SO2 y NOx medidas en los últimos dos años, georeferenciación de las calderas y número de identificación de dichas fuentes y el código de establecimiento respectivo en el Registro de Emisiones y Transferencias de Contaminantes, RETC. Se eximen de este artículo las calderas reguladas por la Norma de Emisión para Centrales Termoeléctricas, D.S. N°13, de 2011, del Ministerio del Medio Ambiente, ya que se encuentran obligadas a declarar sus calderas por esta norma. La Superintendencia del Medio Ambiente mantendrá la información consolidada y sistematizada para efectos de su respectiva fiscalización

15. Plazos excesivos para disponer de información diaria de los contaminantes, también, para los contaminantes que deban cumplir con límites de emisión en masa

Artículo 31. No podrán acogerse al artículo anterior, aquellas instalaciones que reúnan una o más de las siguientes condiciones: a. Instalaciones que se encuentran a menos de 500 metros de distancia de grupos poblados, cursos de aguas, cultivos o áreas sensibles definidas por la correspondiente normativa vigente. b. Instalaciones que almacenen graneles sólidos dispersables que contengan sustancias tóxicas de acuerdo a lo dispuesto en la normativa vigente. En dicho caso deberá asegurarse la total hermeticidad del sistema de confinamiento. c. Instalaciones que almacenen graneles sólidos del tipo D1, D2 y D3, en las que deberá asegurarse la total hermeticidad del sistema de confinamiento. Este debe disponer asimismo de un sistema de ventilación y filtros con un diseño adecuado, los cuales deberán funcionar durante las operaciones de manipulación (carga o descarga). d. Sin perjuicio de lo señalado, se deberá dar cumplimiento según corresponda, a las exigencias establecidas en el D.S. 148, de 12 de junio de 2003, que establece el Reglamento Sanitario sobre Manejo de Residuos Peligrosos y en el D.S. 43, de 27 de julio de 2015, Reglamento de Almacenamiento de Sustancias Peligrosas, ambos del Ministerio de Salud, o aquellos que los reemplacen.

16. El obligar a una empresa a reducir sus emisiones no se debe llamar compensación, pues induce a pensar que el daño se subsana con una acción distinta a la que genera el daño. Sin embargo, se utiliza para decir que se reducirá la contaminación como forma de compensación, lo cual no tiene sentido.

Artículo 48. Para efectos de lo dispuesto en este capítulo, los proyectos o actividades y sus modificaciones, que se sometan o deban someterse al Sistema de Evaluación de Impacto Ambiental, y que deban compensar sus emisiones, deberán presentar al ingresar al Sistema de Evaluación de Impacto Ambiental la estimación de sus emisiones de contaminantes a la atmósfera (al menos para MP10, MP2,5, SO2 , NOx y COVs); la metodología utilizada; y un anexo con la memoria de cálculo. Estos proyectos o actividades, en el marco de la evaluación ambiental, deberán presentar un programa preliminar de compensación de emisiones, cuyo contenido será al menos el siguiente:

a) Estimación anual de las emisiones del proyecto en la fase de construcción, operación y cierre, señalando año y etapa a compensar en que se prevé se superará el umbral indicado en la Tabla 15 para los contaminantes que correspondan.
b) Las medidas de compensación, que deberán cumplir los siguientes criterios:
i. Medibles, esto es, que permitan cuantificar la reducción de las emisiones que se produzca a consecuencia de ellas.
ii. Verificables, esto es, que generen una reducción de emisiones que se pueda cuantificar con posterioridad a su implementación.
iii. Adicionales, entendiendo por tal que las medidas propuestas no respondan a otras obligaciones a que esté sujeto el titular, o bien, que no correspondan a una acción que conocidamente será llevada a efecto por la autoridad pública o particulares.
iv. Permanentes, entendiendo por tal que la rebaja permanezca por el período en que el proyecto está obligado a reducir emisiones.
c) Forma, oportunidad y ubicación en coordenadas WGS84, de su implementación, con un indicador de cumplimiento del programa de compensación.
d) Carta Gantt, que considere todas las etapas para la implementación de la compensación de emisiones y la periodicidad con que informará a la Superintendencia del Medio Ambiente sobre el estado de avance de las actividades comprometidas.

17. Si se instalan instrumentos de medición de última generación, para medir todos gases al interior de las empresas, para se fiscalizados en línea por la SMA, los inventarios de emisiones de las localidades quedarán actualizados, en línea. Por lo tanto, este artículo no tiene sentido:

Artículo 59. Corresponderá a la SEREMI del Medio Ambiente, actualizar el inventario de emisiones en las comunas de Concón, Quintero y Puchuncaví anualmente para las fuentes industriales que representan el 80% de las emisiones de MP, NOx y SO2 y cada 5 años para el inventario completo de fuentes emisoras.

18. Plazo excesivo, de un año, para que la ciudadanía tenga acceso a los datos de mediciones de todos los contaminantes ambientales. Se espera que en 40 días, las nuevas estaciones de monitoreo EMRP y todos los instrumentos de medición continua para todas las fuentes emisoras de las empresa y plataformas web queden operativas.

Artículo 60. Contados 12 meses desde la publicación del presente decreto, la Seremi de Medio Ambiente deberá implementar una plataforma de información a la ciudadanía que contenga al menos los siguientes parámetros: a) Monitoreo de calidad del aire en línea. b) Monitoreo de emisiones en línea. c) Información meteorológica y de ventilación.

19. Los avances de PPDA a la ciudanía debe ser cada 15 días no anual, a través de una plataforma web.

> Artículo 61. La SEREMI del Medio Ambiente, en un plazo de tres meses a partir de la entrada en vigencia del Plan, elaborará un programa de involucramiento comunitario y educación ambiental en el cual se deberá informar a la ciudadanía, al menos una vez al año, respecto de los avances del Plan.

20. No se definen en el PPDA normas de emisión, ni normas de calidad primaria ni secundaria para los COV´ y emanaciones generadas las empresas que componen el cordón industrial de cada localidad. Esto es básico de disponer, pues la SMA a través del RETC dispone de la mayor parte de las emisiones de todas las empresas y debe avanzar con el MINSAL en determinar las nuevas normas, para lo que no este normado.

Existen más omisiones, falencias e incongruncias, esta en sólo una lista incial, para ser considerada en el nuevo PPDA. Pues, el objetivo final del PPDA debe ser solucionar, eficaz y eficientemente, los problemas de contaminación ambiental de Quintero, Puchuncaví y Concón, dadas las consecuencias inmediatas, a mediano y largo plazo, en la salud de la población.