

8. REGULATIONS AND ADVISORIES

The international and national regulations and guidelines regarding benzene in air, water, and other media are summarized in Table 8-1.

ATSDR has derived an acute-duration inhalation MRL of 0.009 ppm for benzene based on a LOAEL of 10.2 ppm for immunological effects in mice exposed for 6 hours/day for 6 consecutive days (Rozen et al. 1984). The LOAEL of 10.2 ppm was adjusted from intermittent to continuous exposure ($LOAEL_{ADJ}=2.55$ ppm) and converted to a human equivalent concentration ($LOAEL_{HEC}=2.55$ ppm) using EPA (1994b) methodology for a category 3 gas; an uncertainty factor of 300 (10 for use of a LOAEL, 3 for extrapolation from animals to humans using dosimetric conversion, and 10 to protect sensitive individuals) was applied.

ATSDR has derived an intermediate-duration inhalation MRL of 0.006 ppm for benzene based on a LOAEL of 10 ppm for significantly delayed splenic lymphocyte reaction to foreign antigens evaluated in *in vitro* mixed lymphocyte reaction following the exposure of male C57Bl/6 mice to benzene vapors for 6 hours/day, 5 days/week for 20 exposure days (Rosenthal and Snyder 1987). The concentration was adjusted from intermittent to continuous exposure ($LOAEL_{ADJ}=1.8$ ppm) and converted to a human equivalent concentration ($LOAEL_{HEC}=1.8$ ppm) using EPA (1994b) methodology for a category 3 gas; an uncertainty factor of 300 (10 for the use of LOAEL, 3 for extrapolation from animals to humans using dosimetric conversion, and 10 for human variability) was applied.

ATSDR has derived a chronic-duration inhalation MRL of 0.003 ppm for benzene based on the results of benchmark dose (BMD) modeling of B cell counts in workers of shoe manufacturing industries in Tianjin, China (Lan et al. 2004a). The resulting $BMCL_{0.25sd}$ of 0.10 ppm was adjusted from intermittent to continuous exposure ($BMCL_{0.25sdADJ}=0.03$ ppm) using EPA (1994b) methodology; an uncertainty factor of 10 (to protect sensitive individuals) was applied.

ATSDR has derived a chronic-duration oral MRL of 0.0005 mg/kg/day for benzene based on estimation of equivalent chronic-duration oral dosing that would result in effects similar to those observed in the occupationally-exposed workers assessed by Lan et al. (2004a, 2004b). The $BMCL_{0.25sdADJ}$ of 0.03 ppm (0.096 mg/m³) was converted to an equivalent $BMDL_{0.25sdADJ}$ of 0.014 mg/kg/day for ingested benzene using EPA (1988b) human reference values for inhalation rate (20 m³/day) and body weight (70 kg) and a factor of 0.5 to adjust for differences in absorption of benzene following inhalation versus oral exposure;

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Table 8-1. Regulations and Guidelines Applicable to Benzene

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification	Group 1 ^a	IARC 1987, 2004, 2007
WHO	Air quality guidelines	6x10 ⁻⁶ unit risk	WHO 2000
	Drinking water quality guidelines	0.01 mg/L ^b	WHO 2004
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (TWA)	0.5 ppm ^c	ACGIH 2006
	STEL	2.5 ppm ^c	
EPA	Hazardous air pollutant	Yes	EPA 2004b 42 USC 7412
NAS/NRC	AEGL-1 ^d		EPA 2005a
	10 minutes	130 ppm	
	30 minutes	73 ppm	
	60 minutes	52 ppm	
	4 hours	18 ppm	
	8 hours	9.0 ppm	
	AEGL-2 ^d		
	10 minutes	2,000 ppm ^e	
	30 minutes	1,100 ppm	
	60 minutes	800 ppm	
	4 hours	400 ppm	
	8 hours	200 ppm	
	AEGL-3 ^d		
	10 minutes	9,700 ppm ^f	
	30 minutes	5,600 ppm ^e	
60 minutes	4,000 ppm ^e		
4 hours	2,000 ppm ^e		
8 hours	990 ppm		
NIOSH	REL (10-hour TWA)	0.1 ppm ^g	NIOSH 2005
	STEL	1.0 ppm ^g	
	IDLH	500 ppm ^g	
OSHA	PEL (8-hour TWA) for general industry	1 ppm	OSHA 2005b, 2005e 29 CFR 1910.1000 29 CFR 1910.1028
	PEL (8-hour TWA) for construction industry	1 ppm	

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Agency	Description	Information	Reference
<u>NATIONAL</u> (cont.)			
OSHA	PEL (8-hour TWA) for shipyard industry	1 ppm	OSHA 2005a,2005b 29 CFR 1915.1000 29 CFR 1915.1028
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act	Yes	EPA 2005b 40 CFR 116.4
	Drinking water standards and health advisories		EPA 2004a
	1-day health advisory for a 10-kg child	0.2 mg/L	
	10-day health advisory for a 10-kg child	0.2 mg/L	
	DWEL	0.1 mg/L	
	10 ⁻⁴ Cancer risk	0.1 mg/L	
	National primary drinking water standards		EPA 2002a
	MCLG	Zero	
	MCL	0.005 mg/L	
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	10 pounds	EPA 2005c 40 CFR 117.3
	Water quality criteria for human health consumption of:		EPA 2002b
	Water + organism	2.2 µg/L ^h	
	Organism only	51 µg/L ^h	
c. Food			
FDA	Bottled drinking water	0.005 mg/L	FDA 2004 21 CFR 165.110
d. Other			
ACGIH	Carcinogenicity classification	A1 ⁱ	ACGIH 2006
	Biological exposure indices (end of shift)		
	S-phenylmercapturic acid in urine	25 µg/g creatinine	
	<i>t,t</i> -Muconic acid in urine	500 µg/g creatinine	
EPA	Carcinogenicity classification	Group A ⁱ	IRIS 2007
	Oral slope factor	1.5x10 ⁻² –5.5x10 ⁻² per (mg/kg)/day	
	Inhalation unit risk	2.2x10 ⁻⁶ –7.8x10 ⁻⁶ per µg/m ³	
	RfC	0.03 mg/m ³	
	RfD	4x10 ⁻³ mg/kg/day	

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Agency	Description	Information	Reference
NATIONAL (cont.)			
EPA	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance		EPA 2005d 40 CFR 302.4
	Reportable quantity	10 pounds ^k	
	RCRA hazardous waste number	U019	
	Effective date of toxic chemical release reporting	01/01/87	EPA 2005e 40 CFR 372.65
NTP	Carcinogenicity classification	Known human carcinogen	NTP 2005

^aGroup 1: carcinogenic to humans

^bFor substances that are considered to be carcinogenic, the guideline value is the concentration in drinking water associated with an upper-bound excess lifetime cancer risk of 10^{-5} (one additional cancer per 100,000 of the population ingesting drinking water containing the substance at the guideline value for 70 years). Concentrations associated with upper-bound estimated excess lifetime cancer risks of 10^{-4} and 10^{-6} can be calculated by multiplying and dividing, respectively, the guideline value by 10.

^cSkin notation: refers to the potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, either by contact with vapors or, of probable greater significance, by direct skin contact with the substance.

^dAEGL-1 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. AEGL-2 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape. AEGL-3 is the airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

^eValues denoted as having safety considerations against the hazard of explosion, whereas the Lower Explosive Limit (LEL) =14,000 ppm and each value should be $\geq 10\%$ LEL.

^fValue denoted as having extreme safety considerations against the hazard of explosion must be taken into account, whereas the LEL =14,000 ppm and each value should be $\geq 50\%$ LEL.

^gNIOSH potential occupational carcinogen

^hThis criterion is based on carcinogenicity of 10^{-6} risk.

ⁱA1: confirmed human carcinogen

^jGroup A: known human carcinogen

^kDesignated CERCLA hazardous substance pursuant to Section 311(b)(2) and 307(a) of the Clean Water Act, Section 112 of the Clean Air Act, and Section 3001 of RCRA.

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = Acute Emergency Exposure Guideline Levels; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DWEL = drinking water equivalent level; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; NAS/NRC = National Academy of Sciences/National Research Council; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; RCRA = Resource Conservation and Recovery Act; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; STEL = short-term exposure limit; TLV = threshold limit values; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization

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an uncertainty factor of 30 (10 to protect sensitive individuals and 3 for uncertainty in route-to-route extrapolation) was applied.

EPA (IRIS 2007) derived an inhalation reference concentration (RfC) for benzene of 0.03 mg/m³ (0.009 ppm) based on the results of BMD modeling of absolute lymphocyte (ALC) data from the occupational epidemiologic study of Rothman et al. (1996a), in which workers were exposed to benzene by inhalation. The resulting BMCL of 7.2 ppm for decreased lymphocyte count was converted to 23.0 mg/m³ and adjusted from intermittent to continuous exposure (BMCL_{ADJ}=8.2 mg/m³); a total uncertainty factor of 300 (3 for effect-level extrapolation, 10 to protect sensitive individuals, 3 for subchronic-to-chronic extrapolation, and 3 for database deficiencies) was applied.

EPA (IRIS 2007) derived an oral reference dose (RfD) for benzene of 0.004 mg/kg/day, based on the results of BMD modeling of ALC data from the occupational epidemiologic study of Rothman et al. (1996a), in which workers were exposed to benzene by inhalation. The resulting BMCL of 7.2 ppm for decreased lymphocyte count was converted to 23.0 mg/m³ and adjusted from intermittent to continuous exposure (BMCL_{ADJ}=8.2 mg/m³). Route-to-route extrapolation methodology was applied to convert from inhalation to equivalent oral exposure, resulting in an equivalent oral dose rate of 1.2 mg/kg/day. This value was divided by a total uncertainty factor of 300 (3 for effect-level extrapolation, 10 to protect sensitive individuals, 3 for subchronic-to-chronic extrapolation, and 3 for database deficiencies).

The International Agency for Research on Cancer (IARC) classifies benzene as a Group 1 carcinogen (carcinogenic to humans) (IARC 2004). EPA classified benzene in Category A (known human carcinogen) based on convincing evidence in humans supported by evidence from animal studies. Under EPA's most recent guidelines for carcinogen risk assessment, benzene is characterized as a known human carcinogen for all routes of exposure based on convincing human evidence as well as supporting evidence from animal studies (IRIS 2007). The National Toxicology Programs lists benzene as a "substance known to be carcinogenic," that is, a substance for which the evidence from human studies indicates that there is a causal relationship between exposure to the substance and human cancer (NTP 2005).

The EPA has a current maximum contaminant level (MCL) of 0.005 mg/L for benzene in drinking water (EPA 2002a). The World Health Organization (WHO) has established a guideline value of 0.01 mg/L for benzene in drinking water (WHO 2004).

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Benzene is on the list of chemicals in "The Emergency Planning and Community Right-to-Know Act of 1986" (EPA 2005d). Section 313 of Title III of the Superfund Amendments and Reauthorization Act (SARA) requires owners and operators of certain facilities that manufacture, import, process, or otherwise use the chemicals on this list to report annually any release of those chemicals to any environmental media over a specified threshold level (U.S. Congress 1986).

OSHA requires employers of workers who are occupationally exposed to benzene to institute engineering controls and work practices to reduce and maintain employee exposure at or below permissible exposure limits (PEL). If an employer can document that benzene is used in the workplace <30 days/year, the employer can use any combination of engineering controls, work practice controls, or respirators to reduce employee exposure to or below the PEL of 1 ppm (8-hour TWA). Respirators must be provided and used during the time period necessary to install or implement feasible engineering and work practice controls, or where controls are not yet sufficient. Respirators are also required when the employer determines that compliance with the PEL is not feasible with engineering or work practice controls, such as maintenance and repair activities, vessel cleaning, or other operations where exposures are intermittent and limited in duration, and in emergencies (OSHA 2005c).

ACGIH limits exposure to benzene to 0.5 ppm (8-hour TWA) (ACGIH 2006). The National Institute for Occupational Safety and Health (NIOSH 2005) has established a recommended exposure level (REL) of 0.1 ppm (15-minute ceiling limit).