

8. REGULATIONS, ADVISORIES, AND GUIDELINES

MRLs are substance specific estimates, which are intended to serve as screening levels, are used by ATSDR health assessors and other responders to identify contaminants and potential health effects that may be of concern at hazardous waste sites.

ATSDR has derived an acute-duration oral MRL of 8×10^{-3} mg/kg/day based on a LOAEL of 2.5 mg/kg/day for hyperactivity in rat offspring whose mothers were exposed to hexachlorobenzene for 4 days prior to mating (Goldey and Taylor 1992).

ATSDR has derived an intermediate-duration oral MRL of 1×10^{-4} mg/kg/day based on degenerative changes in the ovaries of female monkeys exposed to hexachlorobenzene doses ≥ 0.01 mg/kg/day for 90 days (Babineau et al. 1991; Bourque et al. 1995; Jarrell et al. 1993).

ATSDR has derived a chronic-duration oral MRL of 7×10^{-5} mg/kg/day based on a LOAEL of 0.022 mg/kg/day for peribiliary lymphocytosis and fibrosis of the liver in adult F₁ generation male rats fed hexachlorobenzene for 130 weeks in a 2-generation study (Arnold et al. 1985).

The EPA (IRIS 2003) has derived an oral reference dose (RfD) of 8×10^{-4} mg/kg/day for hexachlorobenzene based on a NOAEL of 0.08 mg/kg/day for liver effects in the Arnold et al. (1985) rat chronic feeding study. An uncertainty factor of 100 was used (10 for intraspecies variability and 10 for interspecies extrapolation). No reference concentration (RfC) for chronic inhalation exposures to hexachlorobenzene was reported.

The International Agency for Research on Cancer (IARC) classifies hexachlorobenzene as Group 2B carcinogen (*possibly carcinogenic to humans*) (IARC 2015). The National Toxicology Program (NTP) concluded that hexachlorobenzene is *reasonably anticipated to be a human carcinogen* (NTP 2014). EPA has classified hexachlorobenzene in weight-of-evidence Group B2 (*probable human carcinogen*) (IRIS 2003). EPA derived an oral slope factor of 1.6 per (mg/kg)/day and an inhalation unit risk of 4.6×10^{-4} per ($\mu\text{g}/\text{m}^3$) based on hepatocellular carcinoma in female Sprague-Dawley rats exposed orally. The American Conference of Governmental Industrial Hygienists (ACGIH) has classified hexachlorobenzene as an A3 carcinogen (*confirmed animal carcinogen with unknown relevance to humans*) (ACGIH 2014).

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Although no Occupational Safety and Health Administration (OSHA) standards exist for hexachlorobenzene, the ACGIH (2014) has set a threshold limit value (8-hour time-weighted average) of 0.002 mg/m³, based on a route-to-route extrapolation from an oral study in Rhesus monkeys (Rozman et al. 1978).

Hexachlorobenzene is on the list of chemicals designated Hazardous Air Pollutants (HAPs) under Section 112 of the Clean Air Act (EPA 2013a). Hexachlorobenzene also appears on the list of chemicals in "The Emergency Planning and Community Right-to-Know Act of 1986" (EPCRA) and has been assigned a reportable quantity (RQ) limit of 10 pounds (EPA 2014d). Section 313 of Title III of EPCRA requires owners and operators of certain facilities that manufacture, import, process, or otherwise use the chemicals on this list to report annually their release of those chemicals to any environmental media.

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

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Table 8-1. Regulations, Advisories, and Guidelines Applicable to Hexachlorobenzene

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification	2B ^a	IARC 2015
WHO	Air quality guidelines	No data	WHO 2010
	Drinking water quality guidelines	No guideline value ^b	WHO 2011
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)	0.002 mg/m ³ ^c	ACGIH 2014
AIHA	ERPGs	No data	AIHA 2014
DOE	PAC-1 ^d	0.006 mg/m ³	DOE 2012a
	PAC-2 ^d	8.9 mg/m ³	
	PAC-3 ^d	160 mg/m ³	
EPA	AEGLs	No data	EPA 2014a
	Hazardous air pollutant	Yes	EPA 2013a 42 USC 7412
	NAAQS	No data	EPA 2012c
NIOSH	REL (10-hour TWA)	No data	NIOSH 2015
	IDLH	No data	
OSHA	PEL (8-hour TWA) for general industry	No data	OSHA 2013 29 CFR 1910.1000, Table Z-1
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act	No data	EPA 2013b 40 CFR 116.4
	Drinking water standards and health advisories		EPA 2012b
	1-day health advisory for a 10-kg child	0.05 mg/L	
	10-day health advisory for a 10-kg child	0.05 mg/L	
	DWEL	0.03 mg/L	
	10 ⁻⁴ Cancer risk	0.002 mg/L	

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Agency	Description	Information	Reference
NATIONAL (<i>cont.</i>)			
EPA	National primary drinking water standards	No data	EPA 2009b
	MCL	0.001 mg/L	
	Potential health effects from long-term exposure above the MCL	Liver or kidney problems; reproductive difficulties; increased risk of cancer	
	Common sources of contaminant in drinking water	Discharge from metal refineries and agricultural chemical factories	
	Public Health Goal	Zero	
	National recommended water quality criteria: human health for the consumption of		EPA 2013c
	Water plus organism	0.28 mg/L ^{e,f}	
	Organism only	0.29 mg/L ^{e,f}	
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	No data	EPA 2013d 40 CFR 117.3
	c. Food		
FDA	EAFUS	No data ^g	FDA 2013
d. Other			
ACGIH	Carcinogenicity classification	A3 ^h	ACGIH 2014
EPA	Carcinogenicity classification	B2 ⁱ	IRIS 2003
	RfC	No data	
	RfD	8x10 ⁻⁴ mg/kg/day	
	Inhalation unit risk	4.6x10 ⁻⁴ per µg/m ³	
	Oral slope factor	1.6 per mg/kg/day	
	Identification and listing of hazardous waste	U127	EPA 2013e 40 CFR 261, Appendix VIII
	Inert pesticide ingredients in pesticide products	No data	EPA 2014c
	Superfund, emergency planning, and community right-to-know		EPA 2014d 40 CFR 302.4
	Designated CERCLA hazardous substance and reportable quantity	10 pounds ^j	
	Effective date of toxic chemical release reporting	01/01/1987	EPA 2014e 40 CFR 372.65
EPA	Extremely hazardous substances and its threshold planning quantity	No data	EPA 2013f 40 CFR 355, Appendix A
	TSCA chemical lists and reporting periods	No data	EPA 2014f 40 CFR 712.30

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Agency	Description	Information	Reference
NATIONAL (<i>cont.</i>)			
EPA	TSCA health and safety data reporting	No data	EPA 2014g 40 CFR 716.120
NTP	Carcinogenicity classification	Reasonably anticipated to be a human carcinogen	NTP 2014

^aGroup 2B: possibly carcinogenic to humans.

^bThe WHO noted that when hexachlorobenzene is detected in drinking water, it occurs at concentrations well below those at which toxic effects might be expected, and considered it unnecessary to establish a guideline value. PAC-1: mild, transient health effects. PAC-2: irreversible or other serious health effects that could impair the ability to take protective action. PAC-3: life-threatening health effects.

^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.

^dDefinitions of PAC terminology are available from U.S. Department of Energy (DOE 2012b).

^eThis criterion based on carcinogenicity of 10^{-6} risk and has been revised to reflect the EPA's $q1^*$ or RfD, as contained in IRIS as of May 17, 2002. The fish tissue bioconcentration factor (BCF) from the 1980 Ambient Water Quality Criteria document was retained in each case.

^fEPA has updated its national recommended water quality criteria for human health. The comment period for the draft water quality criteria ended August 13, 2014. A final update has not been issued yet, but the proposed criteria for hexachlorobenzene is 0.0064 mg/L for water + organism and 0.0064 mg/L for organism only (EPA 2014b).

^gThe EAFUS list of substances contains ingredients added directly to food that FDA has either approved as food additives or listed or affirmed as GRAS.

^hA3: confirmed animal carcinogen with unknown relevance to humans

ⁱB2: probable human carcinogen

^jDesignated CERCLA hazardous substance pursuant to Section 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 exposure guideline levels; AIHA = American Industrial Hygiene Association; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; DOE = Department of Energy; DWEL = drinking water equivalent level; EAFUS = Everything Added to Food in the United States; EPA = Environmental Protection Agency; ERPG = emergency response planning guidelines; FDA = Food and Drug Administration; GRAS = Generally Recognized As Safe; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; NAAQS = National Ambient Air Quality Standards; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PAC = Protective Action Criteria; PEL = permissible exposure limit; RCRA = Resource Conservation and Recovery Act; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; TLV = threshold limit values; TSCA = Toxic Substances Control Act; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization