

8. REGULATIONS, ADVISORIES, AND GUIDELINES

MRLs are substance-specific estimates that are intended to serve as screening levels. They 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 inhalation MRL of 2 ppm (7.6 mg/m³) for toluene based on a LOAEL for minimally adverse neurological effects in a susceptible human population (Little et al. 1999).

ATSDR has derived a chronic-duration inhalation MRL of 1 ppm (3.8 mg/m³) for toluene based on a NOAEL for neurological effects in humans in series of studies by the same group of investigators (Schäper et al. 2003, 2004, 2008; Seeber et al. 2004, 2005; Zupanic et al. 2002)

ATSDR has derived an acute-duration oral MRL of 0.8 mg/kg/day for toluene based on a LOAEL for neurological effects in rats (Dyer et al. 1988).

ATSDR has derived an intermediate-duration oral MRL of 0.2 mg/kg/day for toluene based on a NOAEL for immune depression in mice (Hsieh et al. 1989, 1990a, 1991).

The International Agency for Research on Cancer (IARC) has classified toluene as a Group 3 carcinogen (*not classifiable as to its carcinogenicity to humans*) based on the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals (IARC 2013). The World Health Organization (WHO) has not established any air quality guidelines but have 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 (WHO 2010). WHO has established a health-based drinking water guideline for toluene at 0.7 mg/L (WHO 2011).

The EPA and ACGIH also state that there are inadequate data on which to classify toluene in terms of its carcinogenicity in humans or animals (ACGIH 2013; IRIS 2007). Therefore, toluene is assigned the cancer category A4 (*not classifiable as a human carcinogen*) by ACGIH and Group D (*not classifiable as to human carcinogenicity*) by EPA (ACGIH 2013; IRIS 2007). The National Toxicology Program (NTP) has not classified toluene as a carcinogen (NTP 2016).

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The EPA's reference concentration (RfC) for toluene is 5 mg/m³ and the EPA's reference dose (RfD) is 0.08 mg/kg/day (IRIS 2007).

OSHA sets permissible exposure limits (PELs) to protect workers against adverse health effects resulting from exposure to hazardous substances. The PELs determined for hazardous substances are enforceable, regulatory limits on allowable air concentrations in the workplace. OSHA requires employers of workers who are occupationally exposed to these hazardous substances to institute engineering controls and work practices to reduce and maintain employee exposure at or below the PEL. An employer must ensure that an employee's exposure to toluene in any 8-hour work shift of a 40-hour week does not exceed the 8-hour TWA of 200 ppm (OSHA 2013b). The acceptable ceiling concentration for toluene that shall not be exceeded at any time during an 8-hour shift is 300 ppm (OSHA 2013b). The acceptable maximum peak above the ceiling for an 8-hour shift is 500 ppm for 10 minutes (OSHA 2013b).

The ACGIH (2013) recommends an 8-hour TWA Threshold Limit Value (TLV) of 20 ppm toluene to protect against visual impairment and female reproductive effects including pregnancy loss. NIOSH has established a recommended exposure limit (REL) of 100 ppm that should not be exceeded at any time (NIOSH 2011). NIOSH has also established a short-term exposure limit (STEL) of 150 ppm and an immediately dangerous to life or health (IDLH) value of 500 ppm (NIOSH 2011).

Toluene is regulated as a hazardous air pollutant (EPA 2014a) and is subject to the emission limitations for various processes and operations in the synthetic organic chemicals manufacturing industry.

The American Industrial Hygiene Association (AIHA) and the Department of Energy (DOE) have established values for responding to potential releases of airborne toluene for use in community emergency planning. The values established by AIHA (2013) and the DOE (2012) are the Emergency Response Planning Guidelines (ERPGs-1, -2, -3) and Protective Active Criteria (PAC-1, -2, and -3), respectively. The ERPG-1, -2, and -3 values are 50, 300, and 1,000 ppm, respectively, and the PAC-1, -2, and -3 values are 200, 1,200, and 4,500 ppm, respectively, represent increasing severity of effects (mild, irreversible, and life threatening, respectively) for a 1-hour exposure (AIHA 2013; DOE 2012).

Toluene is listed as a chemical that must meet the requirements of Section 313 of Title III of the Superfund Amendments and Reauthorization Act (SARA) (EPA 1996a). Title III of SARA, also known as "The Emergency Planning and Community Right-to-Know Act of 1986," requires owners and operators of certain facilities that manufacture, import, process, or otherwise use the chemicals on this list

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to report annually any release of those chemicals to any environmental media over a specified threshold level (EPA 2013f).

Toluene has been designated as a hazardous substance pursuant to the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) of 1980 (EPA 1995). The statutory source for this designation is Section 311(b)(4) of the Clean Water Act (CWA), Section 307 (a) of the CWA, Section 112 of the Clean Air Act (CAA), and Section 300 of the Resource Conservation and Recovery Act (RCRA) (EPA 2013f). The owner and operator of any facility that produces, uses, or stores a CERCLA hazardous substance is required to immediately report releases to any environmental media, if the amount released is equal to or exceeds the specified “reportable quantity” assigned to the substance. The reportable quantity for toluene is 1,000 pounds (454 kg) (EPA 2013g).

Because of its potential to cause adverse health effects in exposed people, toluene is also regulated by the drinking water standards set by the EPA. Toluene generally gets into drinking water by improper waste disposal or leaking underground storage tanks. In order to protect humans from the risk of developing adverse health effects from exposure to toluene through drinking water, the EPA Drinking Water Regulations and Health Advisories (EPA 2012) lists the maximum contaminant level (MCL) and the maximum contaminant level goal (MCLG) for toluene as 1 mg/L. The FDA set a limit of 1 mg/L in bottled water (FDA 2013).

Under the Toxic Substances Control Act (TSCA), toluene is on the list of chemicals that manufacturers and importers must report for each plant site at which they manufactured or imported toluene during the reporting period specified (EPA 2013l). In accordance with the Federal Hazardous Substances Act (FHSA), manufacturers are required to include special warning labels on some products containing toluene (CPSC). If a product contains $\geq 5\%$ toluene by weight, labels of “Danger”, “Vapor harmful”, and “Poison” with a skull and crossbones must be used. If a product contains $\geq 10\%$ toluene by weight, labels must also include “Harmful or fatal if swallowed” and “Call physician immediately”.

The international and national regulations, advisories, and guidelines regarding toluene 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 Toluene

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification	Group 3 ^a	IARC 2013
WHO	Air quality guidelines	Group 2 ^b	WHO 2010
	Drinking water quality guidelines	0.7 mg/L ^c	WHO 2011
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV-TWA	20 ppm	ACGIH 2013
AIHA	ERPG-1 ^{d,e}	50 ppm	AIHA 2013
	ERPG-2	300 ppm	
	ERPG-3	1,000 ppm	
DOE	PAC-1 ^f	200 ppm	DOE 2012
	PAC-2	1,200 ppm	
	PAC-3	4,500 ppm	
EPA	AEGL-1 ^g		EPA 2013c
	10-minutes	200 ppm	
	30-minutes	200 ppm	
	60-minutes	200 ppm	
	4-hours	200 ppm	
	8-hours	200 ppm	
	AEGL-2 ^g		
	10-minutes	3,100 ppm ^h	
	30-minutes	1,600 ppm ^h	
	60-minutes	1,200 ppm	
	4-hours	790 ppm	
	8-hours	650 ppm	
	AEGL-3 ^g		
	10-minutes	13,000 ppm ⁱ	
	30-minutes	6,100 ppm ^h	
60-minutes	4,500 ppm ^h		
4-hours	3,000 ppm ^h		
8-hours	2,500 ppm ^h		
	Hazardous air pollutant	Yes	EPA 2014a 42 USC 7412
NIOSH	NAAQS	No data	EPA 2014d
	REL	100 ppm	NIOSH 2011
	STEL	150 ppm	
	IDLH	500 ppm	

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NATIONAL (cont.)			
OSHA	PEL (8-hour TWA) for general industry	200 ppm	OSHA 2013b 29 CFR 1910.1000, Table Z-2
	Acceptable ceiling concentration	300 ppm	
	Acceptable maximum peak above the acceptable ceiling concentration for an 8-hour shift	500 ppm for 10 minutes	
	Highly hazardous chemicals	No data	OSHA 2013a 29 CFR 1910.119, Appendix A
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act	Yes	EPA 2013d 40 CFR 116.4
	Drinking water contaminant candidate list	No data	EPA 2009a 74 FR 51850
	Drinking water standards and health advisories		EPA 2012
	MCL	1 mg/L	
	MCLG	1 mg/L	
	Health advisory for 1 day for 10-kg child	20 mg/L	
	Health advisory for 10 days for 10-kg child	2 mg/L	
	DWEL	3 mg/L	
	National primary drinking water standards		EPA 2009b
	MCL	1 mg/L	
	Potential health effects from long-term exposure above the MCL	Nervous system, kidney, or liver problems	
	Common sources of contaminant in drinking water	Discharge from petroleum factories	
	Public Health Goal	1 mg/L	
	National recommended water quality criteria: human health for the consumption of (at 10 ⁻⁴ risk)		EPA 2014e
	Water + organism	1.3 mg/L	
Organism only	15 mg/L		
Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	1,000 pounds	EPA 2013f 40 CFR 117.3	

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NATIONAL (cont.)			
c. Food			
FDA	Bottled water	1 mg/L	FDA 2013 21 CFR 165.110
	EAFUS ^j	No data	FDA 2014
d. Other			
ACGIH	Carcinogenicity classification BEI	A4 ^k	ACGIH 2013
	Toluene in blood; prior to last shift of workweek	0.02 mg/L	
	Toluene in urine; end of shift	0.03 mg/L	
	o-Cresol in urine; end of shift	0.3 mg/g creatinine	
CPSC	Federal Hazardous Substances Act		CPSC 2017
	Labels of "Danger", "Vapor harmful", and "Poison" with a skull and crossbones must be used	≥5% toluene (by weight)	
	Above labels plus "Harmful or fatal if swallowed" and "Call physician immediately" must be used	≥10% toluene (by weight)	
EPA	Carcinogenicity classification	Group D ^l	IRIS 2007
	RfC	5 mg/m ³	
	RfD	0.08 mg/kg/day	
	Identification and listing of hazardous waste	U220	EPA 2013e 40 CFR 261, Appendix VIII
	Inert pesticide ingredients in pesticide products approved for nonfood use only	Yes	EPA 2014b
	Master Testing List	Yes ^m	EPA 2014c
	RCRA waste minimization PBT priority chemical list	No data	EPA 1998 63 FR 60332
	Standards for owners and operators of hazardous waste TSD facilities; groundwater monitoring list	Yes	EPA 2013j 40 CFR 264, Appendix IX
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance and reportable quantity pursuant to Section 311(b)(2) of the Clean Water Act, Section 307(a) of the Clean Water Act, Section 112 of the Clean Air Act, and Section 3001 of RCRA	1,000 pounds	EPA 2013g 40 CFR 302.4

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Agency	Description	Information	Reference
NATIONAL (cont.)			
EPA	Effective date of toxic chemical release reporting	01/01/1987	EPA 2013h 40 CFR 372.65
	Extremely hazardous substances and its threshold planning quantity	No data	EPA 2013i 40 CFR 355, Appendix A
	TSCA chemical lists and reporting periods	No data	EPA 2013k 40 CFR 712.30
	TSCA health and safety data reporting		EPA 2013l
	Effective date	10/04/1982	40 CFR 716.120
	Reporting date	10/04/1992	
NTP	Carcinogenicity classification	No data	NTP 2016

^aGroup 3: not classifiable as to its carcinogenicity to humans.

^bGroup 2 includes pollutants of potential interest, but WHO concluded further investigation would be needed before it was clear whether there was sufficient evidence to warrant their inclusion in the guidelines at present (WHO 2010).

^cConcentrations of the substance at or below the health-based guideline value may affect the appearance, taste, or odor of the water, leading to consumer complaints (WHO 2011).

^dERPG-1: maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing other than mild transient adverse health effects or perceiving a clearly defined, objectionable odor; ERPG-2: maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing irreversible or other serious health effects or symptoms which could impair an individual's ability to take protective action; ERPG-3: maximum airborne concentration below which it is believed that nearly all individuals could be exposed for up to 1 hour without experiencing or developing life-threatening health effects (AIHA 2013).

^eOdor should be detectable near ERPG-1.

^fPAC-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 (DOE 2012).

^gLower Explosive Limit (LEL) = 14,000 ppm.

^hFor values denoted as safety considerations against the hazard(s) of explosion(s) must be taken into account; $\geq 10\%$ LEL.

ⁱFor values denoted as extreme safety considerations against the hazard(s) of explosion(s) must be taken into account; $\geq 50\%$ LEL.

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

^kA4: not classifiable as a human carcinogen.

^lGroup D: not classifiable as to human carcinogenicity.

^mVoluntary chemical testing program underway for SIDS including pharmacokinetic and immunological health effects (EPA 2014c).

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = acute exposure guideline levels; AIHA = American Industrial Hygiene Association; BEI = biological exposure indices; 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; FR = Federal Register; GRAS = generally recognized as safe; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; LEL = lower explosive limit; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; 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; PBT = persistent, bioaccumulative, and toxic; PEL = permissible exposure limit; RCRA = Resource Conservation and Recovery Act; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; SIDS = Screening Information Data Set; STEL = short-term exposure limit; TLV = threshold limit values; TSCA = Toxic Substances Control Act; TSD = treatment, storage, and disposal; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization