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 0.007 mg/kg/day for endosulfan based on a NOAEL of 0.7 mg/kg/day for neurological signs in rabbits (MacKenzie et al. 1981). The MRL was derived by dividing the NOAEL of 0.7 mg/kg/day by an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

ATSDR has derived an intermediate-duration oral MRL of 0.005 mg/kg/day for endosulfan based on a NOAEL of 0.45 mg/kg/day for immunological effects in rats (Banerjee and Hussain 1986). The MRL was derived by dividing the NOAEL of 0.45 mg/kg/day by an uncertainty factor of 100 (10 for animal to human extrapolation and 10 for human variability).

ATSDR has adopted the intermediate-duration oral MRL for endosulfan for the chronic-duration oral MRL.

The EPA (IRIS 2002) has derived an oral reference dose (RfD) of 0.006 mg/kg/day for endosulfan based on a NOAEL of 0.6 mg/kg/day for reduced body weight gain in male and female rats and increased incidence of marked progressive glomerulonephrosis and blood vessel aneurysms in male rats in a 2-year 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 endosulfan was reported. EPA's Office of Chemical Safety and Pollution Prevention (EPA 2010b) derived a chronic population-adjusted dose (cPAD) of 0.006 mg/kg/day based on the same data from which EPA's RfD was derived.

The EPA, the International Agency for Research on Cancer (IARC), and the National Toxicology Program (NTP) have not classified endosulfan as to its carcinogenicity (IARC 2015; IRIS 2002; NTP 2014). The American Conference of Governmental Industrial Hygienists (ACGIH) has classified endosulfan as an A4 carcinogen (*not classifiable as a human carcinogen*) (ACGIH 2014).

Endosulfan, endosulfan sulfate, α-endosulfan, and β-endosulfan have been designated as a hazardous substances pursuant to the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) of 1980 (EPA 201d). The statutory source for this designation for endosulfan sulfate, α-, and β-isomers is Section 307 of the Clean Water Act (CWA). In addition to Section 307(a) of the CWA, the designation for endosulfan is based on Section 311(b)(2) of the CWA, and Section 3001 of the Resource Conservation and Recovery Act (RCRA) (EPA 2014d). The owner and operator of any facility that produces, uses, or stores a CERCLA hazardous substance in an amount exceeding the "threshold planning quantity" are required to immediately report any release to any environmental media, if the amount released is equal to or exceeds the specified "reportable quantity" assigned to the substance. As a hazardous substance that is formulated as a solid, endosulfan is subject to either of two threshold planning quantities (EPA 2013d). If a solid hazardous substance exits in powdered form and has a particle size less than 100 micrometers, then it is subject to the lower number. If the solid does not meet this criterion, then it is subject to the higher number. The threshold reporting quantities for endosulfan are 10 and 10,000 pounds (EPA 2013d). The reportable quantity for endosulfan and its metabolites is 1 pound (EPA 2013d).

Endosulfan is designated as a hazardous substance under Section 311 of the CWA; any discharge of these chemicals over a specified threshold level (10 pounds) into navigable waters is subject to reporting requirements (EPA 2013c).

Between June 27, 1974 and January 18, 1989, the Occupational Safety and Health Administration (OSHA) had promulgated protective, permissible exposure limits (PELs) for approximately 264 toxic substances (OSHA 1993). The OSHA PELs were established 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 indoor air concentrations. OSHA requires employers of workers who are occupationally exposed to these hazardous air contaminants to institute engineering controls and work practices to reduce and maintain employee exposure at or below PELs. An employer must ensure that an employee's exposure in any 8-hour work shift of a 40-hour week does not exceed the 8-hour time-weighted average (TWA) established for the air contaminant (OSHA 2013). On January 18, 1989, OSHA promulgated more protective PELs for approximately 376 toxic substances. Endosulfan was included among 164 toxic substances not previously regulated (OSHA 1989). The newly established PEL for endosulfan was set at 0.1 mg/m^3 (OSHA 1989). OSHA also provided a "skin designation" for endosulfan. Because the 1989 promulgation was rescinded by the 11th Circuit Court Appeals in July 1992, only those PELs in place prior to the 1989 rule are currently enforced by OSHA. On June 30,

1993, OSHA published in the Federal Register a final rule announcing the revocation of the 1989 exposure limits, including the newly established limits for endosulfan (OSHA 1993). Currently, there is no OSHA PEL for endosulfan. However, the National Institute for Occupational Safety and Health (NIOSH) and several states adopted the 0.1 mg/m^3 exposure limit for endosulfan that was initially promulgated by OSHA (NIOSH 1992, 2015).

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

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

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification	No data	IARC 2015
WHO	Air quality guidelines	No data	WHO 2010
	Drinking water quality guidelines		WHO 2011
	Endosulfan	No data[a]	
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)		ACGIH 2014
	Endosulfan[b,c]	0.1 mg/m^3	
AIHA	ERPGs	No data	AIHA 2014
DOE	PAC-1[d]		DOE 2012a
	Endosulfan	0.1 mg/m^3	
	PAC-2[d]		
	Endosulfan	0.8 mg/m^3	
	PAC-3[d]		
	Endosulfan	280 mg/m^3	
EPA	AEGLs	No data	EPA 2014a
	NAAQS	No data	EPA 2012h
NIOSH	REL (10-hour TWA)		NIOSH 2015
	Endosulfan[e]	0.1 mg/m^3	
	IDLH		
	Endosulfan	No data	
OSHA	PEL (8-hour TWA) for general industry	No data	OSHA 2013 29 CFR 1910.1000, Table Z-1
	PEL (8-hour TWA) for construction		OSHA 2014a
	Endosulfan[e]	0.1 mg/m^3	29 CFR 1916.55, Appendix A
	PEL (8-hour TWA) for shipyards		OSHA 2014b
	Endosulfan[e]	0.1 mg/m^3	29 CFR 1915.1000
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act		EPA 2013a 40 CFR 116.4
	Endosulfan	Yes	
	Drinking water standards and health advisories	No data	EPA 2012g
	Master Testing List	No data	EPA 2014b

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

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	National primary drinking water standards	No data	EPA 2009
	National recommended water quality criteria: freshwater and saltwater		EPA 2013b
	α-Endosulfan and β-endosulfan		
	Freshwater CMC (acute)[f,g]	0.22 µg/L	
	Freshwater CCC (chronic)[f,g]	0.056 µg/L	
	Saltwater CMC (acute)[f,g]	0.034 µg/L	
	Saltwater CCC (chronic)[f,g]	0.0087 µg/L	
	National recommended water quality criteria: human health for the consumption		
	Endosulfan sulfate, α-endosulfan, and β-endosulfan		
	Water plus organism[h]	62 µg/L	
	Organism only[h]	89 µg/L	
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act		EPA 2013c 40 CFR 117.3
	Endosulfan	1 pound	
c. Food			
FDA	EAFUS[i]	No data	FDA 2013
d. Other			
ACGIH	Carcinogenicity classification		ACGIH 2014
	Endosulfan	A4[j]	
EPA	Carcinogenicity classification	No data	IRIS 2002
	RfC	No data	
	RfD		
	Endosulfan	0.006 mg/kg/day	
	Inert pesticide ingredients in pesticide products	No data	EPA 2014c
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance and reportable quantity		EPA 2014d 40 CFR 302.4
	Endosulfan[k]	1 pound	
	Endosulfan sulfate[l]	1 pound	
	α-Endosulfan[l]	1 pound	
	β-Endosulfan[l]	1 pound	
	Effective date of toxic chemical release reporting	No data	EPA 2014e 40 CFR 372.65

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

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
	Extremely hazardous substances and its threshold planning quantity Endosulfan		EPA 2013d 40 CFR 355, Appendix A
	Reportable quantity	1 pound	
	Threshold planning quantity	10/10,000 pounds	
NTP	Carcinogenicity classification	No data	NTP 2014

[a]Endosulfan occurs in drinking-water at concentrations well below those at which toxic effects may occur.
[b]Inhalable fraction and vapor is noted because endosulfan exerts sufficient vapor pressure such that it may be present in both particle and vapor phases, with each contributing a significant portion of the dose at the TLV-TWA concentration.
[c]Skin: refers to the potential significant contribution to the overall exposure by the cutaneous route.
[d]Definitions of PAC terminology are available from U.S. Department of Energy (DOE 2012b).
[e]Skin designation
[f]The CMC is an estimate of the highest concentration of a material in surface water to which an aquatic community can be exposed briefly without resulting in an unacceptable effect. The CCC is an estimate of the highest concentration of a material in surface water to which an aquatic community can be exposed indefinitely without resulting in an unacceptable effect. The CMC and CCC are just two of the six parts of an aquatic life criterion; the other four parts are the acute averaging period, chronic averaging period, acute frequency of allowed exceedance, and chronic frequency of allowed exceedance. Because 304(a) aquatic life criteria are national guidance, they are intended to be protective of the vast majority of the aquatic communities in the United States.
[g]This value was derived from data for endosulfan and is most appropriately applied to the sum of α-endosulfan and β-endosulfan.
[h]This criterion has been revised to reflect The EPA's q1* or RfD, as contained in IRIS as of May 17, 2002.
[i]The EAFUS list of substances contains ingredients added directly to food that FDA has either approved as food additives or listed or affirmed as GRAS.
[j]A4: not classifiable as a human carcinogen
[k]Designated CERCLA hazardous substance pursuant to Section 311(b)(2) and Section 307(a)of the Clean Water Act and Section 3001 of RCRA.
[l]Designated CERCLA hazardous substance pursuant to Section 307(a)of the Clean Water Act.

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = acute exposure guideline levels; AIHA = American Industrial Hygiene Association; CCC = criterion continuous concentration; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; CMC = criteria maximum concentration; DOE = Department of Energy; 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; 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; TWA = time-weighted average; WHO = World Health Organization