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.

An MRL of 0.001 ppm ($1x10^{-3}$ ppm) has been derived for acute-duration inhalation exposure (≤14 days) to glutaraldehyde. The MRL is based on a NOAEL of 0.125 ppm and a LOAEL of 0.25 ppm for histopathological nasal lesions in male F344 rats exposed to glutaraldehyde vapor for a single 6-hour period (Gross et al. 1994; NTP 1993). The NOAEL of 0.125 ppm was duration-adjusted to simulate a 24-hour exposure (0.125 ppm x 6 hours/24 hours = $NOAEL_{ADJ}$ of 0.031 ppm) and converted to a HEC ($NOAEL_{HEC}$ = 0.003 ppm) according to EPA (1994) cross-species dosimetric methodology for a category 1 gas where inhalation exposure-related effects occur within the extrathoracic region of the respiratory tract. A total uncertainty factor of 3 (1 for extrapolation from animals to humans using dosimetric adjustment and 3 for sensitive individuals) was applied.

An MRL of 0.00003 ppm ($3.0x10^{-5}$ ppm) has been derived for intermediate-duration inhalation exposure (15–364 days) to glutaraldehyde. BMD analysis was applied to incidence data for female B6C3F1 mice with inflammation in the nasal vestibule/anterior nares following exposure to glutaraldehyde vapor 6 hours/day, 5 days/week for 13 weeks (NTP 1993). A 10% change from control incidence was selected as the BMR. The resulting 95% lower confidence limit on the maximum likelihood estimate of the exposure concentration associated with the selected BMR ($BMCL_{10}$) of 0.0034 ppm was adjusted to simulate a continuous exposure scenario (0.0034 ppm x 6 hours/24 hours x 5 days/7 days = $BMCL_{10ADJ}$ of 0.0006 ppm). Derivation of a HEC based on the $BMCL_{10ADJ}$ of 0.0006 ppm was performed according to EPA (1994) cross-species dosimetric methodology for a category 1 gas where inhalation exposure-related effects occur within the extrathoracic region of the respiratory tract (the nasal cavity in the case of glutaraldehyde), resulting in a $BMCL_{10HEC}$ of 0.00008 ppm ($8x10^{-5}$ ppm). A total uncertainty factor of 3 (1 for extrapolation from animals to humans using dosimetric adjustment and 3 for human variability) was applied.

An MRL of 0.1 mg/kg/day has been derived for chronic-duration oral exposure (365 days or more) to glutaraldehyde. The MRL is based on a NOAEL of 4 mg/kg/day and a LOAEL of 17 mg/kg/day for gastric irritation (multifocal color change, mucosal thickening, nodules, and ulceration affecting primarily the nonglandular mucosa) in male F344 rats administered glutaraldehyde in the drinking water for 2 years

(van Miller et al. 2002). The NOAEL of 4 mg/kg/day was divided by a total uncertainty factor of 30 (10 for extrapolation from animals to humans and 3 for human variability).

IARC has not classified glutaraldehyde as to its carcinogenicity (IARC 2013). The World Health Organization (WHO) has not established any air quality or drinking water guidelines for glutaraldehyde (WHO 2010, 2011).

OSHA has not established any enforceable standards for glutaraldehyde (OSHA 2017). NIOSH has recommended a ceiling limit of 0.2 ppm that should not be exceeded at any time (NIOSH 2016). ACGIH has recommended a ceiling limit of 0.05 ppm that should not be exceeded at any time (ACGIH 2016).

The American Industrial Hygiene Association (AIHA) and the Department of Energy (DOE) have established identical values for responding to potential releases of airborne glutaraldehyde for use in community emergency planning. The values established by AIHA (2016) and the DOE (2012) are the Emergency Response Planning Guidelines (ERPGs-1, -2, -3) and Protective Active Criteria (PAC-1, -2, and -3), respectively. These values (0.2, 1, and 5 ppm) represent increasing severity of effects (mild, irreversible, and life-threatening, respectively) for a 1-hour exposure.

EPA and NTP have not classified glutaraldehyde as a carcinogen. The EPA has not derived an oral reference dose (RfD) or an inhalation reference concentration (RfC) for glutaraldehyde (IRIS 2013). ACGIH (2016) has classified glutaraldehyde as an A4 carcinogen (*not classifiable as a human carcinogen*).

Under the Toxic Substances Control Act (TSCA), glutaraldehyde is on the list of chemicals that manufacturers and importers must report for each plant site at which they manufactured or imported glutaraldehyde during the reporting period specified (EPA 2012i, 2012j).

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

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

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification	No data	IARC 2013
WHO	Air quality guidelines	No data	WHO 2010
	Drinking water quality guidelines	No data	WHO 2011
NATIONAL			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV-C (ceiling)[a]	0.05 ppm	ACGIH 2016
AIHA	ERPG-1[b,c]	0.2 ppm	AIHA 2016
	ERPG-2	1 ppm	
	ERPG-3	5 ppm	
DOE	PAC-1[d]	0.2 ppm	DOE 2012
	PAC-2	1 ppm	
	PAC-3	5 ppm	
EPA	AEGLs	No data	EPA 2013a
	Second AEGL chemical priority list	No data	EPA 2013b
	Hazardous air pollutant	No data	EPA 2013c 42 USC 7412
	NAAQS	No data	EPA 2013f
NIOSH	REL (ceiling TWA)[e]	0.2 ppm	NIOSH 2016
	IDLH	No data	
OSHA	PEL (8-hour TWA) for general industry	No data	OSHA 2013a 29 CFR 1910.1000, Table Z-1
	Highly hazardous chemicals	No data	OSHA 2013b 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	No data	EPA 2012a 40 CFR 116.4
	Drinking water contaminant candidate list	No data	EPA 2009a 74 FR 51850
	Drinking water standards and health advisories	No data	EPA 2012b
	National primary drinking water standards	No data	EPA 2009b
	National recommended water quality criteria	No data	EPA 2009c

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

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
EPA	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	No data	EPA 2012d 40 CFR 117.3
c. Food			
FDA	EAFUS[f]	Yes	FDA 2013
d. Other			
ACGIH	Carcinogenicity classification	A4[g]	ACGIH 2016
EPA	Carcinogenicity classification	No data	IRIS 2013
	RfC	No data	
	RfD	No data	
	Identification and listing of hazardous waste	No data	EPA 2012c 40 CFR 261, Appendix VIII
	Inert pesticide ingredients in pesticide products approved for nonfood use only	Yes	EPA 2013d
	Master Testing List	No data	EPA 2013e
	RCRA waste minimization PBT priority chemical list	No data	EPA 1998e 63 FR 60332
	Standards for owners and operators of hazardous waste TSD facilities; groundwater monitoring list	No data	EPA 2012e 40 CFR 264, Appendix IX
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance and reportable quantity	No data	EPA 2012f 40 CFR 302.4
	Effective date of toxic chemical release reporting	No data	EPA 2012h 40 CFR 372.65
	Extremely hazardous substances and its threshold planning quantity	No data	EPA 2012g 40 CFR 355, Appendix A
	TSCA chemical lists and reporting periods		EPA 2012i 40 CFR 712.30
	Effective date	09/30/1991	
	Reporting date	11/27/1991	
	TSCA health and safety data reporting		EPA 2012j 40 CFR 716.120
	Effective date	09/30/1991	
	Reporting date	06/30/1998	

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

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
NTP	Carcinogenicity classification	No data	NTP 2014

[a]Based on irritation of upper respiratory tract, skin, and eye; central nervous system impairment. Potential for glutaraldehyde to produce dermal and respiratory sensitization. The TLV-C is an exposure limit that should not be exceeded at any instant during the working exposure.
[b]ERPG-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 2016).
[c]Odor should be detectable near ERPG-1.
[d]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 (DOE 2012).
[e]Testing has not been completed to determine the carcinogenicity of glutaraldehyde; however, the limited studies to date indicate that this substance has chemical reactivity and mutagenicity similar to acetaldehyde and malonaldehyde, therefore, NIOSH recommends that careful consideration should be given to reducing exposures to glutaraldehyde (NIOSH 2016).
[f]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.
[g]A4: not classifiable as a human carcinogen

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; 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; 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; TLV-C = threshold limit value-ceiling; TSCA = Toxic Substances Control Act; TSD = treatment, storage, and disposal; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization