

8. REGULATIONS, ADVISORIES, AND GUIDELINES

MRLs are substance specific estimates, which are intended to serve as screening levels, 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 1×10^{-5} ppm for TDI. The MRL is based on LOAEL of 0.005 ppm for decreases in lung function in healthy volunteers exposed to TDI for 6 hours (Vandenplas et al. 1999). The LOAEL was adjusted to continuous 24-hour exposure (from 6 hours/day) and divided by a total uncertainty factor of 100 (10 for the use of a LOAEL and 10 for human variability). Since there is uncertainty that the MRL would be protective for continuous exposure for 14 days, it is suggested that measured air concentrations should not exceed the MRL of 1×10^{-5} ppm during a 24-hour period.

ATSDR has derived a chronic-duration inhalation MRL of 3×10^{-6} ppm for TDI. The MRL is based on the mean daily exposure level of 0.0012 ppm, which resulted in decreases in lung function in workers at flexible foam producing facilities (Clark et al. 1998). The adverse effect level of 0.0012 ppm was adjusted for intermittent exposure (8 hours/day, 5 days/week) and divided by a total uncertainty factor of 100 (10 for the use of a LOAEL and 10 for human variability).

EPA (IRIS 2003) has derived a chronic-duration RfC of 7×10^{-5} mg/m³ (1×10^{-5} ppm) based on a NOAEL of 0.0009 ppm and a LOAEL of 0.0019 ppm for decreases in lung function in workers at a TDI manufacturing facility (Diem et al. 1982). The NOAEL was adjusted for intermittent exposure ($[10 \text{ m}^3/\text{day}]/[20 \text{ m}^3/\text{day}]$, 5 days/week) and divided by a total uncertainty factor of 30 (3 to account for both extrapolation from a subchronic study and the lack of developmental toxicity data in a second species and 10 for intrahuman variability).

ATSDR has derived a chronic-duration inhalation MRL of 0.001 mg/m³ for polymeric MDI. The MRL is based on a BMCL₁₀ of 0.48 mg/m³ for basal cell hyperplasia in the nasal cavity observed in rats exposed to polymeric MDI for 2 years (Reuzel et al. 1994). The BMCL₁₀ was adjusted for intermittent exposure (6 hours/day, 5 days/week) and multiplied by a regional deposited dose ratio for extrathoracic effect (RDDR_{ET}) of 0.453 to calculate the human equivalent concentration (BMCL_{HEC}). The BMCL_{HEC} of 0.039 mg/m³ was divided by a total uncertainty factor of 30 (3 to extrapolate from animals to humans with dosimetric adjustments and 10 for human variability).

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EPA (IRIS 2002) has derived a chronic-duration RfC of 0.0006 mg/m³ based on a BMCL_{ADJ} of 0.14 mg/m³ for basal cell hyperplasia in rats exposed to polymeric MDI for 2 years (Reuzel et al. 1994). The BMCL_{HEC} was calculated by multiplying the BMCL_{ADJ} of 0.14 mg/m³ by a RDD_{RET} of 0.453. The BMCL_{HEC} of 0.06 mg/m³ was divided by a total uncertainty factor of 100 (10 for intraindividual variation, 3 for the lack of reproductive data, and 3 for “interspecies variation inasmuch as dosimetric adjustments had been made”).

The international and national regulations, advisories, and guidelines regarding toluene diisocyanate and methylenediphenyl diisocyanate 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 Diisocyanate and Methylenediphenyl Diisocyanate

Agency	Description	Information	Reference
<u>International</u>			
Guidelines:			
IARC	Carcinogenicity classification Toluene diisocyanate 4,4'-MDI	Group 2B ^a Group 3 ^b	IARC 2014
WHO	Air quality guidelines Drinking water quality guidelines	Not listed Not listed	WHO 2010 WHO 2011
<u>National</u>			
Regulations and guidelines:			
a. Air			
ACGIH	TLV-TWA ^{c,d} 2,4-TDI 2,6-TDI Monomeric 4,4'-MDI STEL 2,4-TDI 2,6-TDI	0.005 ppm 0.005 ppm 0.005 ppm 0.02 ppm 0.02 ppm	ACGIH 2013
AIHA	ERPG-1 ^e 2,4- and 2,6-TDI Monomeric 4,4'-MDI ERPG-2 ^e 2,4- and 2,6-TDI Monomeric 4,4'-MDI ERPG-3 ^e 2,4- and 2,6-TDI Monomeric 4,4'-MDI	0.01 ppm ^f Not appropriate 0.15 ppm 5 ppm 0.6 ppm 55 ppm	AIHA 2013
DOE	PAC-1 ^g TDI, mixed isomers 2,4-TDI 2,6-TDI Monomeric 4,4'-MDI Polymeric 4,4'-MDI PAC-2 ^g TDI, mixed isomers 2,4-TDI 2,6-TDI Monomeric 4,4'-MDI Polymeric 4,4'-MDI	0.045 ppm 0.020 ppm 0.020 ppm 0.45 mg/m ³ 40 mg/m ³ 0.43 ppm 0.083 ppm 0.083 ppm 5 mg/m ³ 40 mg/m ³	DOE 2012

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Agency	Description	Information	Reference
<u>National (cont.)</u>			
DOE	PAC-3 ^g		
	TDI, mixed isomers	0.43 ppm	
	2,4-TDI	0.51 ppm	
	2,6-TDI	0.51 ppm	
	Monomeric 4,4'-MDI	55 mg/m ³	
NAS	2,4-TDI		NAS/NRC 2004
	AEGL-1 ^h		
	10 minutes	0.020 ppm	
	30 minutes	0.020 ppm	
	60 minutes	0.020 ppm	
	4 hours	0.010 ppm	
	8 hours	0.010 ppm	
	AEGL-2 ^h		NAS/NRC 2004
	10 minutes	0.24 ppm	
	30 minutes	0.17 ppm	
	60 minutes	0.083 ppm	
	4 hours	0.021 ppm	
	8 hours	0.021 ppm	
	AEGL-3 ^h		
	10 minutes	0.65 ppm	
	30 minutes	0.65 ppm	
	60 minutes	0.51 ppm	
	4 hours	0.32 ppm	
	8 hours	0.16 ppm	
	2,6-Toluene diisocyanate		
	AEGL-1 ^h		
	10 minutes	0.020 ppm	
	30 minutes	0.020 ppm	
	60 minutes	0.020 ppm	
	4 hours	0.010 ppm	
	8 hours	0.010 ppm	
	AEGL-2 ^h		
	10 minutes	0.24 ppm	
	30 minutes	0.17 ppm	
	60 minutes	0.083 ppm	
	4 hours	0.021 ppm	
	8 hours	0.021 ppm	

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<u>National</u> (cont.)				
NAS	AEGL-3 ^h			
	10 minutes	0.65 ppm		
	30 minutes	0.65 ppm		
	60 minutes	0.51 ppm		
	4 hours	0.32 ppm		
	8 hours	0.16 ppm		
EPA	Hazardous air pollutant		EPA 2014a	
	2,4-TDI	Yes	42 USC 7412	
	Monomeric 4,4'-MDI	Yes		
	NAAQS	Not listed	EPA 2014d	
NIOSH	REL		NIOSH 2011a,	
	2,4-TDI	Potential occupational carcinogens	2011b	
		Monomeric 4,4'-MDI	0.05 mg/m ³	
	Ceiling limit (10-minute)			
		Monomeric 4,4'-MDI	0.2 mg/m ³	
OSHA	IDLH			
	2,4-Toluene diisocyanate	2.5 ppm		
	Monomeric 4,4'-MDI	75 mg/m ³		
	Ceiling limit (15-minute TWA) for general industry		OSHA 2013b	
	2,4-TDI	0.02 ppm	29 CFR 1910.1000, Table Z-2	
	2,6-TDI	0.02 ppm		
	Monomeric 4,4'-MDI	0.02 ppm		
	Highly hazardous chemicals	Not listed	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	Not listed	EPA 2013a	
	Drinking water contaminant candidate list		40 CFR 116.4	
	TDI (toluene 2,4- (2,6-) diisocyanate)	Yes	EPA 2009a	
			74 FR 51850	
	Drinking water standards and health advisories	Not listed	EPA 2012	
	National primary drinking water standards	Not listed	EPA 2009b	
National recommended water quality criteria: human health for the consumption of (at 10 ⁻⁴ risk)	Not listed	EPA 2014e		

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Agency	Description	Information	Reference
<u>National</u> (cont.)			
EPA	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act	Not listed	EPA 2013c 40 CFR 117.3
c. Food			
FDA	Bottled water	Not listed	FDA 2013 21 CFR 165.110
	EAFUS ⁱ	Not listed	FDA 2014
d. Other			
ACGIH	Carcinogenicity classification		ACGIH 2013
	2,4-TDI	A4 ⁱ	
	2,6-TDI	A4 ⁱ	
EPA	Carcinogenicity classification		IRIS 2002, 2003
	TDI (toluene 2,4- (2,6-) diisocyanate)	No data	
	MDI (monomeric MD) and polymeric MDI)	Group D ^k	
	RfC		
	2,4-/2,6-TDI	7x10 ⁻⁵ mg/m ³	
	MDI (monomeric MDI and polymeric MDI)	6x10 ⁻⁴ mg/m ³	
	RfD		
	2,4-/2,4-TDI (toluene 2,4- (2,6-) diisocyanate)	Not listed	
	MDI (monomeric MDI and polymeric MDI)	Not listed	
	Identification and listing of hazardous waste		EPA 2013c 40 CFR 261, Appendix VIII
	TDI (toluene 2,4- (2,6-) diisocyanate)	U223	
	Master Testing List		EPA 2014c
	Monomeric 4,4'-MDI	Yes ^l	
	Polymethylene polyphenyl isocyanate	Yes ^l	
	Polymeric 4,4'-MDI	Yes ^l	
	RCRA waste minimization PBT priority chemical list	Not listed	EPA 1998b 63 FR 60332

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Agency	Description	Information	Reference
<u>National</u> (cont.)			
EPA	Standards for owners and operators of hazardous waste TSD facilities; groundwater monitoring list	Not listed	EPA 2013d 40 CFR 264, Appendix IX
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance and reportable quantity		EPA 2013e 40 CFR 302.4
	TDI (toluene 2,4- (2,6-) diisocyanate) ^m	100 pounds	
	2,4-TDI ^m	100 pounds	
	2,6-TDI ^m	100 pounds	
	Monomeric 4,4'-MDI ⁿ	5,000 pounds	
	Effective date of toxic chemical release reporting		EPA 2013g 40 CFR 372.65
	TDI (toluene 2,4- (2,6-) diisocyanate)	01/01/1990	
	2,4-TDI	01/01/1987	
	2,6-TDI	01/01/1987	
	Monomeric 4,4'-MDI	01/01/1987	
	Extremely hazardous substances and its threshold planning quantity		EPA 2013f 40 CFR 355, Appendix A
	2,4-TDI	500 pounds	
	2,6-TDI	100 pounds	
	TSCA chemical lists and reporting periods		EPA 2013h 40 CFR 712.30
	Monomeric 4,4'-MDI		
	Effective date	10/29/1990	
	Reporting date	12/27/1990	
	Polymeric 4,4'-DMDI		
Effective date	10/29/1990		
Reporting date	12/27/1990		
TSCA health and safety data reporting		EPA 2013i 40 CFR 716.120	
TDI (2,4 and 2,6 mixed isomers); 2,4-TDI; monomeric 4,4'-MDI; polymeric 4,4'-MDI			
Effective date	06/01/1987		
Reporting date	06/01/1997		
2,6-Toluene diisocyanate			
Effective date	06/01/1987		
Reporting date	12/19/1995		

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<u>National</u> (cont.)			
NTP	Carcinogenicity classification TDI	Reasonably anticipated to be a human carcinogen	NTP 2011

^aGroup 2B: possibly carcinogenic to humans.

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

^cSensitization notation: refers to potential for agent to produce dermal and/or respiratory sensitization (ACGIH 2013).

^dAdopted values and notations are for those for which changes are proposed in the Notice of Intended Changes (ACGIH 2013).

^eERPG-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; and 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).

^fOdor should be detectable near ERPG-1.

^gPAC-1: mild, transient health effects; PAC-2: irreversible or other serious health effects that could impair the ability to take protective action; and PAC-3: life-threatening health effects (DOE 2012).

^hAEGL-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. However, the effects are not disabling and are transient and reversible upon cessation of exposure. 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 (NAS/NRC 2004).

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

^jA4: not classifiable as a human carcinogen.

^kGroup D: not classifiable as to human carcinogenicity.

^lVoluntary chemical testing program underway for SIDS for health and ecological effects and chemical fate (EPA 2014c).

^mDesignated CERCLA hazardous substance and reportable quantity pursuant to Section 112 of the Clean Air Act and Section 3001 of RCRA.

ⁿDesignated CERCLA hazardous substance and reportable quantity pursuant to Section 112 of the Clean Air Act.

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; MDI = methylenediphenyl diisocyanate; 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; TDI = toluene diisocyanate; 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