

## 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.

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

ATSDR has derived an acute-duration oral MRL of 0.2 mg/kg/day based on a NOAEL of 8.5 mg/kg/day for neurotoxicity in rats administered RDX via gavage 7 days/week for 14 days (U.S. Army 2006b). Using a PBPK model, an internal dose metric (peak brain concentration) was simulated and a HED of 6.4547 mg/kg/day was estimated. An uncertainty factor of 30 (3 for animal to human extrapolation with dosimetric adjustment and 10 for human variability) was applied to the  $\text{NOAEL}_{\text{HED}}$ .

ATSDR has derived an intermediate-duration oral MRL of 0.1 mg/kg/day based on a  $\text{BMDL}_{10}$  for neurological effects in rats administered RDX via gavage 7 days/week for 90 days (U.S. Army 2006b). The  $\text{BMDL}_{10}$  was estimated using an internal dose metric to simulate peak brain concentration; a HED of the  $\text{BMDL}_{10}$  was estimated using a PBPK model. The  $\text{BMDL}_{\text{HED}}$  of 4.1308 mg/kg/day was divided by an uncertainty factor of 30 (3 for animal to human extrapolation with dosimetric adjustments and 10 for human variability).

ATSDR has derived a chronic-duration oral MRL of 0.1 mg/kg/day based on a NOAEL of 8 mg/kg/day for neurotoxicity in rats exposed to dietary RDX for 2 years (U.S. Army 1983a). Using a PBPK model, an internal dose metric (peak brain concentration) was simulated and a HED of 4.223 mg/kg/day was estimated. An uncertainty factor of 30 (3 for animal to human extrapolation with dosimetric adjustment and 10 for human variability) was applied to the  $\text{NOAEL}_{\text{HED}}$ .

EPA (IRIS 2009) has derived an oral reference dose (RfD) of 0.003 mg/kg/day based on a NOAEL 0.3 mg/kg/day and LOAEL of 1.5 mg/kg/day for inflammation of the prostate in rats exposed to RDX in the diet for 2 years (U.S. Army 1983a). An uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 to protect against unusually susceptible individuals) was applied to the NOAEL.

## 8. REGULATIONS AND ADVISORIES

**Table 8-1. Regulations and Guidelines Applicable to RDX**

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification	No	IARC 2009
WHO	Air quality guidelines	No	WHO 2000
	Drinking water quality guidelines	No	WHO 2006
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA) <sup>a</sup>	0.5 mg/m <sup>3</sup>	ACGIH 2008
	STEL (15-minute TWA)	No	
	TLV-basis (critical effect)	Liver damage	
AIHA	ERPG values	No	AIHA 2008
EPA	AEGL values	No	EPA 2008a
	Hazardous air pollutant	No	EPA 2009b 42 USC 7412
NIOSH	REL (10-hour TWA)	1.5 mg/m <sup>3</sup>	NIOSH 2005
	STEL (15-minute)	3.0 mg/m <sup>3</sup>	
	IDLH	Not determined	
	Target organs	Eyes, skin, and central nervous system	
OSHA	PEL (8-hour TWA) for general industry	Vacated <sup>b</sup>	OSHA 1993 29 CFR 1910.1000, Final Rule
b. Water			
EPA	Drinking water standards and health advisories		EPA 2006a
	1-day health advisory for a 10-kg child	0.1 mg/L	
	10-day health advisory for a 10-kg child	0.1 mg/L	
	DWEL	0.1 mg/L	
	Lifetime	0.002 mg/L	
	10 <sup>-4</sup> Cancer risk	0.03 mg/L	
	National primary drinking water standards	No	EPA 2003
	National recommended water quality criteria	No	EPA 2006b
c. Food			
FDA	EAFUS	No <sup>c</sup>	FDA 2008

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**Table 8-1. Regulations and Guidelines Applicable to RDX**

Agency	Description	Information	Reference
<u>NATIONAL</u> (cont.)			
d. Other			
ACGIH	Carcinogenicity classification	A4 <sup>d</sup>	ACGIH 2008
EPA	Carcinogenicity classification	Group C <sup>e</sup>	IRIS 2009
	RfC	No	
	RfD	3.0x10 <sup>-3</sup> mg/kg/day	
	Oral slope factor	1.1 mg/kg/day <sup>-1</sup>	
	Superfund, emergency planning, and community right-to-know		
	Designated CERCLA hazardous substance	No	EPA 2009c 40 CFR 302.4
	Effective date of toxic chemical release reporting	No	EPA 2009d 40 CFR 372.65
	TSCA chemical lists and reporting periods		EPA 2009e 40 CFR 712.30
	Effective date	09/29/2006	
	Reporting date	11/28/2006	
	TSCA health and safety data reporting		EPA 2009a 40 CFR 716.120
	Effective date	09/29/2006	
	Sunset date	11/28/2006	
NTP	Carcinogenicity classification	No	NTP 2005

<sup>a</sup>Skin: refers to the potential significant contribution to the overall exposure by the cutaneous route.

<sup>b</sup>On January 19, 1989, OSHA published its final rule on Air Contaminants, which amended 29 CFR 1910.1000 by lowering 212 of OSHA's existing PELs for toxic substances and setting PELs for 164 toxic substances that had been previously unregulated. A PEL value of 1.5 mg/m<sup>3</sup> was adopted for RDX in March 1989. However, on July 7, 1992, the Eleventh Circuit Court of Appeals issued a decision in AFL-CIO vs. OSHA that vacated these revised standards.

<sup>c</sup>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.

<sup>d</sup>A4: not classifiable as a human carcinogen.

<sup>e</sup>Group C: possible human carcinogen, based on hepatocellular adenomas and carcinomas in female B6C3F1 mice.

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; 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; NIOSH = National Institute for Occupational Safety and Health; NTP = National Toxicology Program; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; STEL = short-term exposure limit; TLV = threshold limit values; TSCA = Toxic Substances Control Act; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization