

## 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.

As summarized in Table 8-1, ATSDR has derived individual acute-duration oral MRLs for 6 DNT isomers (2,3-DNT, 2,4-DNT, 2,5-DNT, 2,6-DNT, 3,4-DNT and 3,5-DNT), intermediate-duration oral MRLs for 2,4-DNT and 2,6-DNT, and a chronic-duration oral MRL for 2,4-DNT.

The International Agency for Research on Cancer (IARC) classifies 2,4- and 2,6-DNT as Group 2B carcinogens (*possibly carcinogenic to humans*) and 3,5-DNT as a Group 3 carcinogen (*not classifiable as to its carcinogenicity to humans*) (IARC 2015). The U.S. EPA classifies the 2,4-/2,6-DNT mixture as B2 (*probable human carcinogen*) (IRIS 2003). The American Conference of Governmental Industrial Hygienists (ACGIH) has classified the 2,4-/2,6-DNT mixture as an A3 carcinogen (*confirmed animal carcinogen with unknown relevance to humans*) (ACGIH 2014).

OSHA requires employers of workers who are occupationally exposed to the 2,4-/2,6-DNT mixture to institute engineering controls and work practices to reduce and maintain employee exposure at or below permissible exposure limits (PEL) of 1.5 mg/m<sup>3</sup> (OSHA 2013).

The EPA (IRIS 2002) has derived an oral reference dose (RfD) of 0.002 mg/kg/day for 2,4-DNT based on a NOAEL of 0.2 mg/kg/day for neurotoxicity, Heinz bodies, and biliary tract hyperplasia in Beagle dogs in a 2-year feeding study (Ellis et al. 1985). The EPA (IRIS 2003) also derived an oral slope factor (q1\*) of 0.068 (mg/kg/day)<sup>-1</sup> based on multiple tumor types in female rats (U.S. Army 1979) for the 2,4-/2,6-DNT mixture.

Tg-DNT and 3,4-DNT are on the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) list of hazardous substances and reportable quantities and have been assigned a reportable quantity (RQ) limit of 10 pounds combined (EPA 2014d). 2,4-DNT, and 2,6-DNT also appear on the CERCLA list of chemicals and have been assigned RQ limits of 10 and 100 pounds, respectively (EPA 2014d).

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The 2,4-/2,6-DNT mixture is designated as a hazardous substances under Section 311 of the Clean Water Act; any discharge of these chemicals over a specified threshold level (10 pounds) into navigable waters is subject to reporting requirements (EPA 2013d).

The international and national regulations, advisories, and guidelines regarding DNTs in air, water, and other media are summarized in Table 8-2.

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**Table 8-1. Oral Minimal Risk Levels (MRLs) for Dinitrotoluenes**

Isomer	2,3-DNT	2,4-DNT	2,5-DNT	2,6-DNT	3,4-DNT	3,5-DNT
<b>Acute-duration</b>						
MRL (mg/kg/day)	0.09	0.05	0.007	0.09	0.03	0.03
Critical effect	Kidney and hematopoietic effects in rats	Neurotoxicity in dogs	Splenic lesions in rats	Hematological effects in dogs	Hematopoietic effects in rats	Testicular effects in rats
Point of departure	275 mg/kg/day (LOAEL)	5 mg/kg/day (NOAEL)	2.05 mg/kg/day (BMDL <sub>10</sub> )	9.31 mg/kg/day (BMDL <sub>1SD</sub> )	8.05 mg/kg/day (BMDL <sub>10</sub> )	10 mg/kg/day (NOAEL)
Uncertainty factor <sup>a</sup>	3,000 (10L, 10A, 10H, 3D)	100 (10A, 10H)	300 (10A, 10H, 3D)	100 (10A, 10H)	300 (10A, 10H, 3D)	300 (10A, 10H, 3D)
<b>Intermediate-duration</b>						
MRL (mg/kg/day)		0.007		0.004		
Critical effect		Hematological effects in dogs		Splenic lesions in dogs		
Point of departure		0.67 mg/kg/day (BMDL <sub>1SD</sub> )		4 mg/kg/day (LOAEL)		
Uncertainty factor <sup>a</sup>		100 (10A, 10H)		1000 (10L, 10A, 10H)		
<b>Chronic-duration</b>						
MRL (mg/kg/day)		0.001				
Critical effect		Hematological effects in dogs				
Point of departure		0.12 mg/kg/day (BMDL <sub>1SD</sub> )				
Uncertainty factor <sup>a</sup>		100 (10A, 10H)				

<sup>a</sup>Uncertainty factors are comprised of uncertainty associated with use of a LOAEL (L), extrapolation from animals to humans (A), human variability (H), and/or database limitations (D).

BMDL<sub>10</sub> = lower 95% confidence limit on the benchmark dose (BMD<sub>10</sub>) associated with a response rate that differs from the control response rate by 10%; BMDL<sub>1SD</sub> = lower 95% confidence limit on the benchmark dose (BMD<sub>1SD</sub>) associated with a change of 1 standard deviation from the controls; DNT = dinitrotoluene; LOAEL = lowest-observed-adverse-effect-level; NOAEL = no-observed-adverse-effect level

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**Table 8-2. Regulations, Advisories, and Guidelines Applicable to Dinitrotoluenes**

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification		IARC 2015
	2,4-DNT	Group 2B <sup>a</sup>	
	2,6-DNT	Group 2B <sup>a</sup>	
	3,5-DNT	Group 3 <sup>b</sup>	
WHO	Air quality guidelines	No data	WHO 2010
	Drinking water quality guidelines	No data	WHO 2011
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA)		ACGIH 2014
	DNT <sup>c,d</sup>	0.2 mg/m <sup>3</sup>	
AIHA	ERPGs	No data	AIHA 2014
DOE	PAC-1 <sup>e</sup>		DOE 2012a
	DNT <sup>c</sup> , 2,4-, 2,6-, and 3,4-DNT	0.6 mg/m <sup>3</sup>	
	PAC-2 <sup>e</sup>		
	DNT <sup>c</sup>	1.1 mg/m <sup>3</sup>	
	2,4-DNT	4.9 mg/m <sup>3</sup>	
	2,6-DNT	12 mg/m <sup>3</sup>	
EPA	PAC-3 <sup>e</sup>		EPA 2014a
	DNT <sup>c</sup> , 2,4-, 2,6-, and 3,4-DNT	200 mg/m <sup>3</sup>	
	AEGLs	No data	
	Hazardous air pollutant 2,4-DNT	Yes	
NIOSH	NAAQS	No data	EPA 2014c
	REL (10-hour TWA)		NIOSH 2015
	DNT <sup>c,f,g</sup>	1.5 mg/m <sup>3</sup>	
OSHA	IDLH		OSHA 2013 29 CFR 1910.1000, Table Z-1 OSHA2014a 29 CFR 1926.55, Appendix A OSHA 2014b 29 CFR 1915.1000
	DNT <sup>c,f,g</sup>	50 mg/m <sup>3</sup>	
	PEL (8-hour TWA) for general industry		
	DNT <sup>c,g</sup>	1.5 mg/m <sup>3</sup>	
	PEL (8-hour TWA) for construction		
DNT <sup>c,g</sup>	1.5 mg/m <sup>3</sup>		
	PEL (8-hour TWA) for shipyards		
DNT <sup>c,g</sup>	1.5 mg/m <sup>3</sup>		

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Agency	Description	Information	Reference
<b>NATIONAL</b> ( <i>cont.</i> )			
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act		EPA 2013b 40 CFR 116.4
	DNT <sup>c</sup> , 2,4-, 2,6-, and 3,4-DNT	Yes	
	Drinking water standards and health advisories		EPA 2012b
	1-day health advisory for a 10-kg child		
	2,4-DNT	1 mg/L	
	2,6-DNT	0.4 mg/L	
	10-day health advisory for a 10-kg child		
	2,4-DNT	1 mg/L	
	2,6-DNT	0.04 mg/L	
	DWEL		
	2,4-DNT	0.1 mg/L	
	2,6-DNT	0.04 mg/L	
	10 <sup>-4</sup> Cancer risk		
	2,4-DNT	0.005 mg/L	
	2,6-DNT	0.005 mg/L	
	National primary drinking water standards	No data	EPA 2009
	National recommended water quality criteria: human health for the consumption of		EPA 2013c
	2,4-DNT		
	Water plus organism	0.11 µg/L <sup>h,i</sup>	
	Organism only	3.4 µg/L <sup>h,i</sup>	
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act		EPA 2013d 40 CFR 117.3
	DNT	10 pounds	
c. Food			
FDA	EAFUS <sup>j</sup>	No data	FDA 2013
d. Other			
ACGIH	Carcinogenicity classification		ACGIH 2014
	DNT	A3 <sup>c,k</sup>	
EPA	Carcinogenicity classification		IRIS 2003
	2,4-/2,6-DNT mixture; no CASRN	B2 <sup>l</sup>	
	Oral slope factor		
	2,4-/2,6-DNT mixture; no CASRN	0.68 (mg/kg/day) <sup>-1</sup>	

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Agency	Description	Information	Reference
<b>NATIONAL</b> ( <i>cont.</i> )			
EPA ( <i>cont.</i> )	RfC		IRIS 2002
	2,4-DNT	No data	
	RfD		
	2,4-DNT	0.002 mg/kg/day	
	Identification and listing of hazardous waster		EPA 2013e 40 CFR 261, Appendix VIII
	2,4-DNT	U105	
	2,6-DNT	U106	
	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
	DNT <sup>c</sup> and 3,4-DNT	10 pounds <sup>m</sup>	
	2,4-DNT	10 pounds <sup>n</sup>	
	2,6-DNT	100 pounds <sup>o</sup>	
	Effective date of toxic chemical release reporting		EPA 2014e 40 CFR 372.65
	DNT	01/01/1990	
	2,4-DNT	01/01/1987	
	2,6-DNT	01/01/1987	
	Extremely hazardous substances and its threshold planning quantity	No data	EPA 2014f 40 CFR 355, Appendix A
	TSCA chemical lists and reporting periods		EPA 2014f 40 CFR 712.30
	2,4-DNT		
	Effective date	03/11/1994	
	Reporting date	05/10/1994	
	TSCA health and safety data reporting		EPA 2014g 40 CFR 716.120
2,4-DNT			
Effective date	03/11/1994		
Reporting date	06/30/1998		

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Agency	Description	Information	Reference
<b>NATIONAL</b> ( <i>cont.</i> )			
NTP	Carcinogenicity classification	No data	NTP 2014

<sup>a</sup>Group 2B: possibly carcinogenic to humans.

<sup>b</sup>Group 3: not classifiable as to its carcinogenicity to humans

<sup>c</sup>Tg-DNT is composed primarily of the 2,4- and 2,6-DNT isomers and the other four isomers (2,3-, 2,5-, 3,4-, and 3,5-DNT) make up only 5% of Tg-DNT.

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

<sup>e</sup>Definitions of PAC terminology are available from U.S. Department of Energy (DOE 2012b).

<sup>f</sup>NIOSH potential occupational carcinogen.

<sup>g</sup>Skin designation.

<sup>h</sup>This criterion is based on carcinogenicity of  $10^{-6}$  risk.

<sup>i</sup>EPA has updated its national recommended water quality criteria for human health. The comment period for the draft water quality criteria ended August 13, 2014. A final update has not been issued yet, but the proposed criteria for 2,4-DNT is 0.0378 µg/L for water + organism and 0.711 µg/L for organism only (EPA 2014b).

<sup>j</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>k</sup>A3: confirmed animal carcinogen with unknown relevance to humans.

<sup>l</sup>Group B2: probable human carcinogen.

<sup>m</sup>Designated CERCLA hazardous substance pursuant to Section 311(b)(2) and Section 307(a) of the Clean Water Act.

<sup>n</sup>Designated CERCLA hazardous substance pursuant to Section 311(b)(2) and Section 307(a) of the Clean Water Act, Section 112 of the Clean Air Act, and Section 3001 of RCRA.

<sup>o</sup>Designated CERCLA hazardous substance pursuant to Section 311(b)(2) and Section 307(a) of the Clean Water Act, and Section 3001 of RCRA.

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; DNT = dinitrotoluene; 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; 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; TSCA = Toxic Substances Control Act; TWA = time-weighted average; WHO = World Health Organization