

## 8. REGULATIONS AND ADVISORIES

International and national regulations and guidelines pertinent to human exposure to cresols are summarized in Table 8-1.

ATSDR has derived an intermediate-duration oral MRL of 0.1 mg/kg/day for cresols based on an increase in incidence of nasal lesions in male rats administered *m/p*-cresol in the diet for 13 weeks (NTP 1992b). The MRL was derived using benchmark modeling of incidence data for nasal lesions in male rats. Following EPA's Benchmark Dose Guidance (EPA 2000a) to select a point of departure, a BMR of 10% was selected for the benchmark analysis of nasal lesion incidence data in male rats in the 13-week NTP (1992b) study. The BMD corresponding to a BMR of 10% extra risk is 55.89 mg/kg/day; the corresponding BMDL<sub>10</sub> is 13.94 mg/kg/day. An uncertainty factor of 100 (10 for interspecies extrapolation and 10 for human variability) was applied to the BMDL<sub>10</sub>.

ATSDR has derived a chronic-duration oral MRL of 0.1 mg/kg/day for cresols based on increased incidences of bronchiole hyperplasia of the lung and follicular degeneration of the thyroid gland in female mice administered *m/p*-cresol in the diet for 2 years. The MRL was derived using a LOAEL of 100 mg/kg/day divided by an uncertainty factor of 1,000 (10 for use of a LOAEL, 10 for extrapolation from animals to humans, and 10 for human variability).

EPA (IRIS 2008) has derived oral reference doses of 0.05 mg/kg/day for *m*- and *o*-cresol based on NOAELs of 50 mg/kg/day for decreased body weights and neurotoxicity (myoclonus, tremors, labored respiration) observed in Sprague-Dawley rats exposed by gavage for 90 days (TRL 1986) in an assessment conducted in 1989. An uncertainty factor of 100 (10 for interspecies and 10 for intraspecies variability) was applied to the NOAEL.

The EPA (IRIS 2008) has classified *m*-cresol, *o*-cresol, and *p*-cresol as possible human carcinogens (Group C) based on inadequate human data and limited data in animals. The assessment was based on an increased incidence of skin papillomas in mice in an initiation-promotion study and on the fact that the cresol isomers produced positive results in genetic toxicity studies both alone and in combination. According to EPA's updated criteria for assessing carcinogenicity of chemicals (EPA 2005c), cresols fall in the category of chemicals for which there is "inadequate information to assess carcinogenic potential." The American Conference of Governmental Industrial Hygienists (ACGIH), International Agency for

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

Agency	Description	Information	Reference
<u>INTERNATIONAL</u>			
Guidelines:			
IARC	Carcinogenicity classification	No data	IARC 2004
WHO	Air quality guidelines	No data	WHO 2000
	Drinking water quality guidelines	No data	WHO 2004
<u>NATIONAL</u>			
Regulations and Guidelines:			
a. Air			
ACGIH	TLV (8-hour TWA), all isomers <sup>a</sup>	5 ppm	ACGIH 2005
EPA	AEGL	No data	EPA 2006a
	Hazardous air pollutant, all isomers	Yes	EPA 2006c 42 USC 7412
NIOSH	REL (10-hour TWA), all isomers	2.3 ppm	NIOSH 2005
	IDLH, all isomers	250 ppm	
OSHA	PEL (8-hour TWA) for general industry, all isomers <sup>b</sup>	5 ppm	OSHA 2005c 29 CFR 1910.1000
	PEL (8-hour TWA) for construction industry, all isomers <sup>b</sup>	5 ppm	OSHA 2005b 29 CFR 1926.55, Appendix A
	PEL (8-hour TWA) for shipyard industry, all isomers <sup>b</sup>	5 ppm	OSHA 2005a 29 CFR 1915.1000
b. Water			
EPA	Designated as hazardous substances in accordance with Section 311(b)(2)(A) of the Clean Water Act, all isomers	Yes	EPA 2006b 40 CFR 116.4
	Drinking water standards and health advisories	No data	EPA 2004
	Reportable quantities of hazardous substances designated pursuant to Section 311 of the Clean Water Act, mixed cresols	Yes	EPA 2006f 40 CFR 117.3
	Water quality criteria for human health	No data	EPA 2006e
c. Food			
FDA	Bottled drinking water	No data	FDA 2005 21 CFR 165.110
d. Other			
ACGIH	Carcinogenicity classification	No data	ACGIH 2005
EPA	Carcinogenicity classification		IRIS 2008
	Cresol	No data	
	<i>m</i> -Cresol	Group C <sup>c</sup>	
	<i>o</i> -Cresol	Group C <sup>c</sup>	
	<i>p</i> -Cresol	Group C <sup>c</sup>	

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Agency	Description	Information	Reference
<b>NATIONAL (cont.)</b>			
EPA	RfC		IRIS 2008
	Cresol	No data <sup>d</sup>	
	<i>m</i> -Cresol	No data <sup>d</sup>	
	<i>o</i> -Cresol	No data <sup>d</sup>	
	<i>p</i> -Cresol	No data <sup>d</sup>	
	RfD		
	Cresol	No data	
	<i>m</i> -Cresol	0.05 mg/kg/day	
	<i>o</i> -Cresol	0.05 mg/kg/day	
	<i>p</i> -Cresol	Withdrawn	
	Identification and listing of hazardous waste, mixed cresols	U052	EPA 2006d 40 CFR 261, Appendix VIII
	Superfund, emergency planning, and community right-to-know		EPA 2006g 40 CFR 302.4
	Designated CERCLA hazardous substance, all isomers	Yes	
	Reportable quantity	100 pounds	
	Effective date of toxic chemical release reporting, all isomers	01/01/87	EPA 2006i 40 CFR 372.65
	Extremely hazardous substances and their threshold planning quantities, <i>o</i> -cresol only	1,000/10,000 pounds	EPA 2006h 40 CFR 355, Appendix A
NTP	Carcinogenicity classification	No data	NTP 2004

<sup>a</sup>Skin notation: refers to the potential significant contribution to the overall exposure by the cutaneous route, including mucous membranes and the eyes, either by contact with vapors, liquids, and solids.

<sup>b</sup>Skin designation

<sup>c</sup>Group C: possible human carcinogen

<sup>d</sup>The health effects data for cresol, *m*-cresol, *o*-cresol, and *p*-cresol were reviewed by the U.S. EPA RfD/RfC Work Group and determined to be inadequate for the derivation of an inhalation RfC.

ACGIH = American Conference of Governmental Industrial Hygienists; AEGL = Acute Exposure Guideline Level; CERCLA = Comprehensive Environmental Response, Compensation, and Liability Act; CFR = Code of Federal Regulations; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; 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; TLV = threshold limit values; TWA = time-weighted average; USC = United States Code; WHO = World Health Organization

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Research on Cancer (IARC), and the National Toxicology Program (NTP) have not classified cresols for human carcinogenicity (ACGIH 2005; IARC 2004; NTP 2004).

OSHA requires employers of workers who are occupationally exposed to cresol to institute engineering controls and work practices to reduce and maintain employee exposure at or below permissible exposure limit time-weighted average (PEL-TWA). The employer must use engineering and work practice controls to reduce exposures to or below an 8-hour TWA of 5 ppm for cresol and its isomers (OSHA 2006). Both NIOSH and ACGIH and have established guideline values that range from 2.3 to 5 ppm for cresol and its isomers (ACGIH 2005; NIOSH 2005).

EPA regulates cresols and its isomers under the Clean Air Act (CAA) and the Clean Water Act (CWA) and has designated them as hazardous air pollutants (HAPs) and hazardous substances, respectively (EPA 2006b, 2006c). EPA has established a reportable quantity (RQ) of 100 pounds (EPA 2006i).