8. REGULATIONS AND ADVISORIES

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

An MRL of 1 mg/kg/day was derived for acute-duration oral exposure (#14 days) to DEHP in the 1993 toxicological profile for DEHP. Based on a re-evaluation of the database, including consideration of recent studies, this MRL has been withdrawn. An acute oral MRL is not currently derived for DEHP due to insufficient data on male reproductive effects, a known critical end point based on longer duration studies. In particular, derivation of an acute oral MRL is precluded by a lack of dose-response information on development of the male reproductive system in offspring acutely exposed during gestation and/or lactation. As previously discussed in Reproductive and Developmental Toxicity (Section 2.2, Summary of Health Effects), morphological and other effects in androgen-sensitive tissues, as well as reduced fetal and neonatal testosterone levels and adult sexual behavioral changes, have been observed in male rat offspring exposed to DEHP during gestation and lactation for intermediate durations of exposure.

An MRL of 0.1 mg/kg/day was derived for intermediate-duration (15–364 days) oral exposure to DEHP based on a NOAEL of 14 mg/kg/day for decreased fertility in mice (Lamb et al. 1987). Mice of both sexes were exposed to DEHP in the diet for up to 126 days in a continuous breeding reproductive toxicity study that also found reduced fertility at doses $140 mg/kg/day. This derivation used an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

The Draft for Public Comment version of this profile used a LOAEL of 3.3 mg/kg/day for testicular pathology in male offspring of rats that were exposed to DEHP in drinking water throughout pregnancy and during postnatal days 1–21 (Arcadi et al. 1998) as the basis of a provisional intermediate-duration oral MRL of 0.01 mg/kg/day. The 3.3 mg/kg/day dose was classified as a serious LOAEL and was used to derive the MRL with an uncertainty factor of 300 (10 for the use of a LOAEL, 10 for interspecies extrapolation, and 3 for human variability). A component factor of 3 was used for human variability because DEHP was administered during the most sensitive period during development. The MRL was provisional because it was derived from a serious LOAEL, which is not conventional ASTDR methodology. The Arcadi et al. (1998) study was judged to be inadequate for MRL derivation because the NTP-CERHR Expert Panel on DEHP (NTP 2000b) concluded that the effect levels are unreliable, making them unsuitable for identifying a LOAEL. In particular, NTP (2000b) found that (1) the methods

used to verify and characterize the administered doses were not clearly described or completely reported, and could not be resolved, and (2) the study authors did not reconcile their blood DEHP concentration data with other studies.

In the 1993 toxicological profile for DEHP, an MRL of 0.4 mg/kg/day was derived for intermediate oral exposure to DEHP based on a NOAEL of 44 mg/kg/day for fetal malformations from a developmental toxicity study in mice (Tyl et al. 1988). An uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability) was used in that derivation. This MRL is higher than the intermediate MRL derived in this profile and is based on an inappropriate end point. In particular, the 44 mg/kg/day developmental toxicity NOAEL is no longer a suitably sensitive basis for MRL derivation because of more recent evidence of testicular toxicity at a lower dose (38 mg/kg/day) in rats exposed to DEHP for 90 days (Poon et al. 1997).

An MRL of 0.06 mg/kg/day was derived for chronic-duration ($365 days) oral exposure to DEHP based on a NOAEL of 5.8 mg/kg/day for testicular pathology in male rats that were exposed to DEHP in the diet for up to 104 weeks in a chronic toxicity study (David et al. 2000a). The LOAEL in this study was 29 mg/kg/day for bilateral aspermatogenesis. The chronic MRL was derived by dividing the 5.8 mg/kg/day NOAEL by an uncertainty factor of 100 (10 for extrapolation from animals to humans and 10 for human variability).

The EPA derived a chronic oral RfD of 0.02 mg/kg/day for DEHP based on a LOAEL of 19 mg/kg/day for hepatic effects in guinea pigs fed a diet containing DEHP for 1 year (Carpenter et al. 1953; IRIS 2001).

Table 8-1. Regulations and Guidelines Applicable to DEHP

Agency	Description	Information	Reference
INTERNATIONAL			
Guidelines:			
IARC	Carcinogenicity classification	Group 3[a]	IARC 2001
NATIONAL			
Regulations and Guidelines:			
a. Air:			
ACGIH	TLV-TWA	5 mg/m^3	ACGIH 2001
NIOSH	IDLH REL (10-hour TWA) STEL (15-minute TWA)	5,000 mg/m^3 5 mg/m^3 10 mg/m^3	NIOSH 2001
OSHA	PEL (8-hour TWA)	5 mg/m^3	OSHA 2001b 29CFR1910.1000
	PEL (8-hour TWA) for construction workers	5 mg/m^3	OSHA 2001c 29CFR1926.55
	PEL (8-hour TWA) for shipyard workers	5 mg/m^3	OSHA 2001a 29CFR1915.1000
USC	Listed as a hazardous air pollutant		USC 2001 42 USC 7412
b. Water			
EPA	Drinking water standard	6 µg/L	EPA 2001 40CFR141.32(e)(62)
	Groundwater monitoring Suggested methods 8060 8270	 PQL 20 µg/L 10 µg/L	EPA 2001 40CFR264, Appendix IX
	Health advisories 10^{-4} cancer risk[b] DWEL[c]	 $3x10^{-4}$ µg/L $7x10^{-4}$ µg/L	EPA 2000
	MCL	6 µg/L	EPA 2001 40CFR141.61c
	MCLG	Zero	EPA 2001 40CFR141.50(a)(21)
	Water quality criteria—human health for consumption of: Water and organism Organism only	 1.8 µg/L 5.9 µg/L	EPA 1999

Table 8-1. Regulations and Guidelines Applicable to DEHP *(continued)*

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
c. Food			
FDA	Indirect food additive—acrylic and modified acrylic plastics, semirigid and rigid	Use only as a flow promoter at a level not to exceed 3 weight-percent based on the monomers	FDA 2001h 21CFR177.1010 (a)(8)
	Indirect food additive—component of cellophane used for food packaging	Alone or in combination with other phthalates where total phthalates do not exceed 5%	FDA 2001h 21CFR177.1200(c)
	Indirect food additive—plasticizer in resinous and polymeric coatings used as the food-contact surface of articles intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food		FDA 2001h 21CFR175.300(b)(3)
	Indirect food additive—substances permitted for use in adhesives		FDA 2001h 21CFR175.105(c)(5)
	Indirect food additive—used as a defoaming agent in the manufacture of paper and paperboard intended for use in packaging, transporting, or holding food		FDA 2001h 21CFR176.210(d)(3)
	Indirect food additive—used in surface lubricants employed in the manufacture of metallic articles that contact food	Total residual lubricant remaining on the metallic article not to exceed 0.015 mg/inch^2 of metallic food-contact surface	FDA 2001h 21CFR178.3910 (a)(2)
	Prior-sanctioned food ingredients—classified as a plasticizer, when migrating from food packaging materials	For foods of high water content only	FDA 2001h 21CFR181.27

Table 8-1. Regulations and Guidelines Applicable to DEHP *(continued)*

Agency	Description	Information	Reference
NATIONAL *(cont.)*			
d. Other			
ACGIH	Carcinogenicity classification	A3[d]	ACGIH 2001
DOT	Category D noxious liquid substance	Allowed to be carried by the Coast Guard	DOT 2001 33CFR151.47
EPA	Carcinogenicity classification RfC RfD Oral slope factor Drinking water unit risk	Group B2[e] Not available $2x10^{-2}$ mg/kg/day $1.4x10^{-2}$ mg/kg/day $4x10^{-7}$ $(\mu g/L)^{-1}$	IRIS 2001
	Health based limits for exclusion of waste-derived residues—concentration limits for residues	$3x10^{1}$ mg/kg	EPA 2001 40CFR266, Appendix VII
	Identification and listing of hazardous waste—hazardous waste number	U028	EPA 2001 40CFR261.33
	Reportable quantity of a CERCLA hazardous substance under Section 307(a) of the Clean Water Act, Section 112 of the Clean Air Act, and RCRA Section 3001	100 pounds	EPA 2001 40CFR302.4
	Risk specific doses Unit risk Risk specific dose	 $2.4x10^{-7}$ $\mu g/m^3$ $4.2x10^{1}$ $\mu g/m^3$	EPA 2001 40CFR266, Appendix V
	Toxic chemical release reporting; community right-to-know—effective date for reporting	01/01/87	EPA 2001 40CFR372.65
	TSCA—health and safety data reporting[f] Effective date Sunset date	 10/04/82 10/04/92	EPA 2001 40CFR716.120(c)
	TSCA—testing consent order Testing FR publication date	 Chemical fate 01/09/89	EPA 2001 40CCFR799.5000

Table 8-1. Regulations and Guidelines Applicable to DEHP *(continued)*

Agency	Description	Information	Reference
STATE			
a. Air			
Idaho	Toxic air pollutants carcinogenic increments AACC (annual average) EL	 4.2 µg/m^3 2.8x10^{-2} pounds/hour	ID Dept. of Health & Welfare 1999
New Hampshire	Regulated toxic air pollutant OEL	 5 mg/m^3	BNA 2001
North Carolina	Toxic air pollutant 24-hour chronic toxicant	 0.03 mg/m^3	BNA 2001
Washington	Acceptable source impact levels at 10^{-6} risk (annual average)	2.5 µg/m^3	WA Dept. of Ecology 1998
Wisconsin	Hazardous air contaminants without acceptable ambient concentrations requiring application of best available control technology	250 pounds/year[2]	WI Dept. of Natural Resources 1997
b. Water			
Alaska	MCL	6 µg/L	AK Dept. Environ. Conservation 1999
Arizona	Aquifer water quality standard	6 µg/L	BNA 2001
California	Drinking water standard	4 µg/L	HSDB 2001
	MCL	4 µg/L	CA Dept. of Health Services 2000
Colorado	Groundwater organic chemical standard	6 µg/L	CO Dept. of Public Health & Environ. 1999
Kentucky	Maximum allowable instream concentration	1.8 µg/L	BNA 2001
Maine	Drinking water guideline	25 µg/L	HSDB 2001
New Jersey	Groundwater quality criteria PQL	3 µg/L 30 µg/L	NJ Dept. of Environ. Protection 1993
Rhode Island	Groundwater quality standard Preventive action limit	6 µg/L 3 µg/L	BNA 2001
South Dakota	MCL	6 µg/L	SD Dept. of Environ. & Natural Resources 1998
Vermont	Groundwater quality standard Enforcement standard Preventive action level	 6.0 µg/L 3.0 µg/L	BNA 2001

Table 8-1. Regulations and Guidelines Applicable to DEHP *(continued)*

Agency	Description	Information	Reference
STATE *(cont.)*			
c. Food	No data		
d. Other			
Connecticut	Direct exposure criteria for soil Residential Industrial/commercial	 44 mg/kg 410 mg/kg	BNA 2001
Massachusetts	RfD Oral slope factor	$2x10^{-2}$ mg/kg/day $1.4x10^{-2}$ $(mg/kg/day)^{-1}$	BNA 2001
Minnesota	Slope factor Health risk limit	0.014 $(mg/kg/day)^{-1}$ 20 µg/L	BNA 2001

[a]Group 3: not classifiable as to its carcinogenicity to humans
[b]10^{-4} cancer risk: The concentration of a chemical in drinking water corresponding to an estimated lifetime cancer risk of 1 in 10,000.
[c]DWEL: A lifetime exposure concentration protective of adverse, non-cancer health effects, that assumes all of the exposure to a contaminant is from drinking water.
[d]A3: confirmed animal carcinogen with unknown relevance to humans
[e]Group B2: probable human carcinogen
[f]All chemical substances within a category are subject to all the provisions of part 716 for the time period from the effective date of the category until the sunset date.

AACC = acceptable ambient concentration for a carcinogen; ACGIH = American Conference of Governmental Industrial Hygienists; BNA = Bureau of National Affairs; CERCLA = Comprehensive Environmental Response Compensation and Liability Act; CFR = Code of Federal Regulations; DOT = Department of Transportation; DWEL = drinking water equivalent level; EL = emissions screening level; EPA = Environmental Protection Agency; FDA = Food and Drug Administration; FR = Federal Register; HSDB = Hazardous Substances Data Bank; IARC = International Agency for Research on Cancer; IDLH = immediately dangerous to life or health; IRIS = Integrated Risk Information System; MCL = maximum contaminant level; MCLG = maximum contaminant level goal; NIOSH = National Institute for Occupational Safety and Health; OEL = occupational exposure level; OSHA = Occupational Safety and Health Administration; PEL = permissible exposure limit; PQL = practical quantitation limits; RCRA = Resource Conservation and Recovery Act; REL = recommended exposure limit; RfC = inhalation reference concentration; RfD = oral reference dose; STEL = short-term exposure limit; TLV = threshold limit value; TSCA = Toxic Substances Control Act; TWA = time-weighted average; URF = unit risk factor; USC = United States Code