CHAPTER 1. RELEVANCE TO PUBLIC HEALTH

1.1 OVERVIEW AND U.S. EXPOSURES

Pure pentachlorophenol exists as colorless crystals that are poorly soluble in water, but dissolve in organic solvents such as alcohol, ether, and benzene. Typically, technical-grade pentachlorophenol is 86–90% pure. Contaminants generally consist of other polychlorinated phenols, chlorinated dibenzo-*p*-dioxins (CDDs), and chlorinated dibenzofurans (CDFs), which are formed during the manufacturing process and can impart a darker color to the crystals. To increase its water solubility, pentachlorophenol has often been manufactured and marketed as a sodium salt. Pentachlorophenol was, in the past, one of the most heavily used pesticides in the United States, but it is now regulated as a restricted-use pesticide and is no longer contained in wood-preserving solutions or in insecticides or herbicides available for home and garden use. Its use is restricted to the treatment of utility poles, railroad ties, and wharf pilings. Pentachlorophenol is found in all environmental media as a result of its past widespread use; current releases to the environment are more limited as a result of changing use patterns. In addition, a number of other environmental contaminants, including hexachlorobenzene, pentachlorobenzene, pentachloronitrobenzene, and hexachlorocyclohexane isomers, are known to be metabolized to pentachlorophenol.

Humans may be exposed to pentachlorophenol in occupational settings through inhalation of contaminated workplace air and dermal contact with the compound or with wood products treated with the compound. General population exposure may occur through contact with contaminated environmental media, particularly in the vicinity of wood treatment facilities and hazardous waste sites. Important routes of exposure appear to be inhalation of contaminated air, inhalation exposure to pentachlorophenol that has volatilized from treated wood surfaces, ingestion of contaminated groundwater used as a source of drinking water, ingestion of contaminated food, and dermal contact with contaminated soils or wood products treated with the compound. Children are likely to be exposed to pentachlorophenol by the same routes as adults. In addition, small children are generally more likely than adults to have significant contact with soil and have less concern with hygiene than adults. ATSDR believes that the primary route of human exposure to pentachlorophenol at hazardous waste sites is ingestion of contaminated media, and to a lesser extent, inhalation and dermal contact with contaminated media.

1.2 SUMMARY OF HEALTH EFFECTS

Information on the toxicity of pentachlorophenol primarily comes from oral studies in laboratory animals. These studies have evaluated a wide range of potential endpoints following acute, intermediate, or chronic exposure. More limited information comes from observational studies in humans examining workers at manufacturing facilities, pesticide applicators, sawmill workers, individuals living in log homes treated with pentachlorophenol, and the general populations. Almost half of the human studies are case reports and most studies provide no or limited information on exposure.

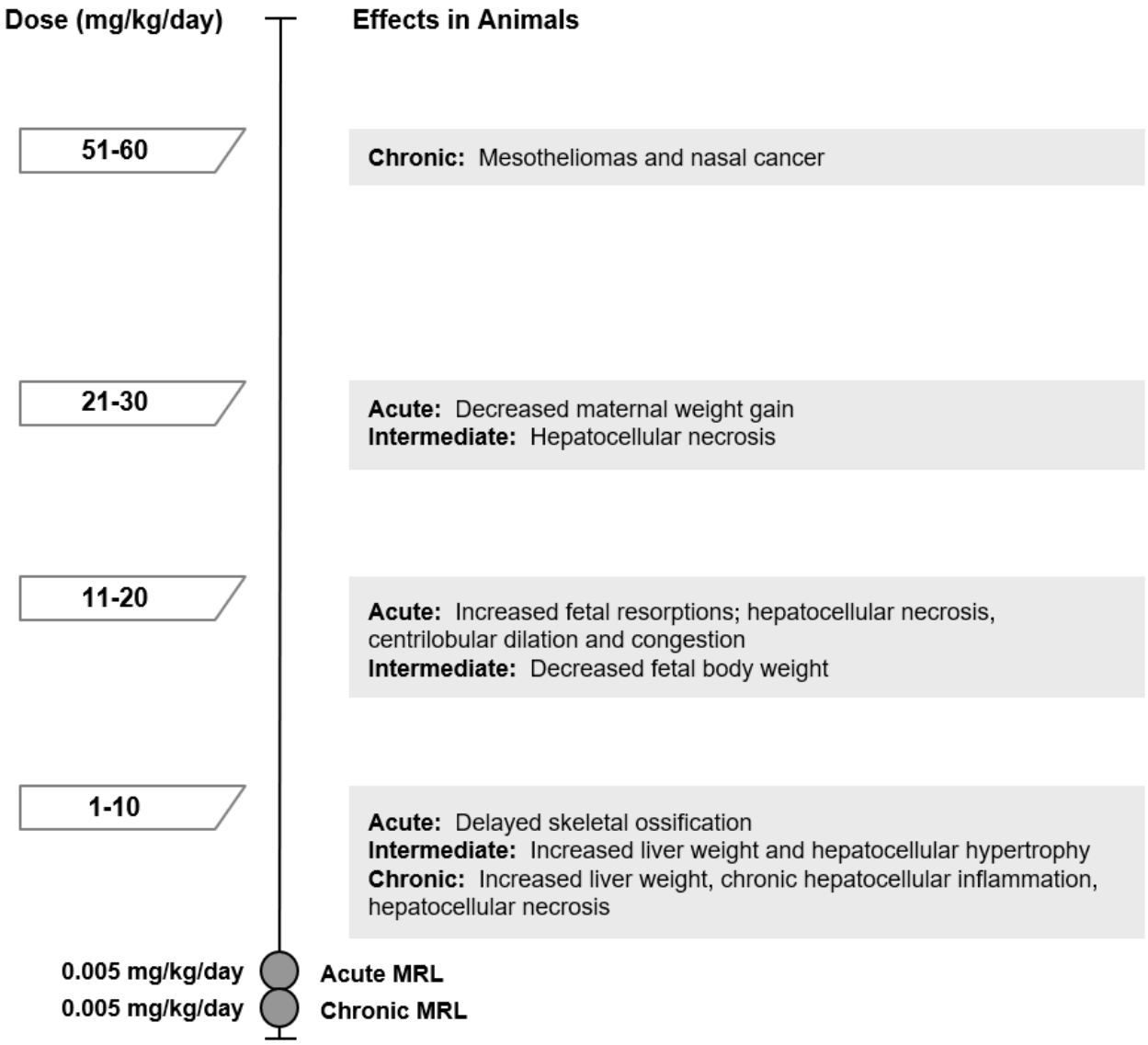
Human studies evaluating the health effects of exposure to pentachlorophenol typically involve exposure to technical-grade pentachlorophenol which contains approximately 85–90% pentachlorophenol and a number of contaminants including other chlorophenols, CDDs, CDFs, hexachlorobenzene, and chlorophenoxy compounds. Studies in laboratory animals have evaluated health effects associated with exposure to pure pentachlorophenol, technical-grade pentachlorophenol, or commercial-grade pentachlorophenol (see Section 2.1 for additional information on the chemical composition of the different grades of pentachlorophenol). Some of the health effects that have been observed in humans and animals have been attributed to the contaminants present in technical-grade and commercial-grade pentachlorophenol rather than the pentachlorophenol itself. The discussion of health effects in this section of the profile excludes health outcomes that have been shown to be due to contaminants.

As illustrated in Figure 1-1, the most sensitive effects in animals appear to be liver damage and developmental toxicity. A systematic review of these endpoints results in the following hazard identification conclusions:

- Hepatic effects are a presumed health effect for humans
- Developmental effects are a presumed health effect for humans

Hepatic Effects. Studies in humans and laboratory animals have identified the liver as a sensitive target of pentachlorophenol toxicity. Inhalation and/or dermal exposures to pentachlorophenol have resulted in alterations in porphyrin excretion (Cheng et al. 1993; Hryhorczuk et al. 1998), liver enlargement (Armstrong et al. 1969; Gordon 1956; Robson et al. 1969; Smith et al. 1996), increased serum liver enzyme levels (Colosio et al. 1993b; Klemmer et al. 1980), and centrilobular degeneration (Bergner et al. 1965) in pentachlorophenol production workers, herbicide sprayers, workers at wood treatment plants, or infants exposed to contaminated diapers and bed linens. These studies provided limited exposure

Figure 1-1. Health Effects Found in Animals Following Oral Exposure to Pentachlorophenol



information. Acute- (Bekhouche et al. 2019; Umemura et al. 1996), intermediate- (Bernard et al. 2002; Greichus et al. 1979; Kerkvliet et al. 1982; Kimbrough and Linder 1978; Knudsen et al. 1974; NTP 1989, 1999; Umemura et al. 1996, 2006), and chronic- (EPA 1997; NTP 1989, 1999; Schwetz et al. 1978) duration oral studies in several laboratory animal species provide strong support for identifying the liver as a target tissue. The effects include alterations in serum liver enzyme levels, increases in liver weight, and hepatocellular hypertrophy, degeneration, fibrosis, and necrosis. These effects were observed after exposure to pure pentachlorophenol, technical-grade pentachlorophenol, and commercial-grade pentachlorophenol.

Developmental Effects. Several epidemiological studies evaluated potential developmental effects in the offspring of male sawmill workers (Dimich-Ward et al. 1996) and the general population (Berghuis et al. 2018; Chen et al. 2013b; Meijer et al. 2008; Roze et al. 2009); however, the results are not consistent across studies. Studies in laboratory animals have reported increases in fetal/neonatal mortality (Bernard and Hoberman 2001; Bernard et al. 2002; Exon and Koller 1982; Schwetz et al. 1974, 1978; Welsh et al. 1987), skeletal malformations (Bernard and Hoberman 2001; Schwetz et al. 1974; Welsh et al. 1987), and decreases in growth (Bernard and Hoberman 2001; Courtney et al. 1976; Larsen et al. 1975; Schwetz et al. 1974).

Cancer Effects. A number of epidemiological cohort and case-control studies have evaluated the potential associations between pentachlorophenol and cancer. In separate evaluations of the available epidemiological data, the Department of Health and Human Services (HHS) (NTP 2016), U.S. Environmental Protection Agency (EPA) (IRIS 2010), and International Agency for Research on Cancer (IARC 2019) concluded that the data suggested an association between pentachlorophenol exposure and increased risk of non-Hodgkin lymphoma based on the consistent findings across epidemiological studies. The data for other cancer types were considered inadequate. In rats, oral exposure to pure pentachlorophenol resulted in increases in the incidence of meostheliomas and nasal squamous cell carcinomas (NTP 1999). Oral exposure to a commercial-grade pentachlorophenol (Dowicide EC-7) or technical-grade pentachlorophenol resulted in hepatocellular adenomas/carcinomas, adrenal pheochromocytomas, and hemangiosarcomas in mice (NTP 1989). Other oral studies have not found increases in tumor incidences in rats exposed to the Dowicide EC-7 commercial-grade pentachlorophenol (NCI 1968; Schwetz et al. 1978).

HHS has categorized pentachlorophenol as “reasonably anticipated to be a human carcinogen” (NTP 2016) and EPA has categorized it as “likely to be carcinogenic to humans” (IRIS 2010). IARC (2019) concluded that pentachlorophenol is “carcinogenic to humans” (Group 1).

1.3 MINIMAL RISK LEVELS (MRLs)

The inhalation database was not considered adequate for deriving inhalation MRLs. The oral database was considered adequate for derivation of acute- and chronic-duration oral MRLs for pentachlorophenol (see Table 1-1). As presented in Figure 1-2, the liver effects and developmental effects were the most sensitive outcomes.

Figure 1-2. Summary of Sensitive Targets of Pentachlorophenol – Oral

The liver and developing fetuses are the most sensitive target of pentachlorophenol oral exposure.

Numbers in circles are the lowest LOAELs for all health effects in animals.
No reliable dose response data were available for humans.

Table 1-1. Minimal Risk Levels (MRLs) for Pentachlorophenol[a]

Exposure duration	MRL	Critical effect	Point of departure	Uncertainty factor	Reference
Inhalation exposure (ppm)					
Acute	Insufficient data for MRL derivation				
Intermediate	Insufficient data for MRL derivation				
Chronic	Insufficient data for MRL derivation				
Oral exposure (mg/kg/day)					
Acute	0.005 (5 µg/kg/day)	Delayed skeletal ossification in rat fetuses	5 (LOAEL)	1,000	Schwetz et al. 1974
Intermediate	Insufficient data for MRL derivation				
Chronic	0.005 (5 µg/kg/day)	Chronic inflammation of the liver in dogs	1.5 (LOAEL)	300	EPA 1997

[a]See Appendix A for additional information.

LOAEL = lowest-observed-adverse-effect level