

Environmental and Human Health Hazards of Five Persistent, Bioaccumulative and Toxic Chemicals

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1. Executive Summary

Section 6(h) of the Toxic Substance Control Act (TSCA), as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act, directs U.S. Environmental Protection Agency (EPA) to take expedited action to propose rules under TSCA with respect to chemicals identified in EPA's 2014 Update of the TSCA Work Plan for Chemical Assessments and meeting criteria relating to persistence, bioaccumulation and toxicity (PBT) and other factors. EPA must issue a proposed rule no later than June 22, 2019, with a final rule to follow no more than 18 months later.

EPA has developed this hazard summary document for five PBT chemical substances it has identified for proposed action under TSCA section 6(h "PBT chemicals"). This document and the data cited for each PBT will support the development of a proposed rule that addresses the risks of injury to the environment and health that the EPA determines are presented by the subject PBT chemicals.

To create this hazard summary, environmental and human health hazard data were compiled from various primary and secondary sources of both confidential and publicly-available information. The hazard summaries relevant to environmental hazard include acute and chronic toxicological information for both aquatic and terrestrial wildlife. Due to a general lack of data found for 2,4,6-Tris(tert-butyl) phenol (2,4,6 TTBP) and pentachlorothiophenol (PCTP) in the primary and secondary sources initially searched, additional literature searches were conducted for environmental hazard data for these chemicals by searching for the chemical name and CASRN in Web of Science and Science Direct. Generally, more acute than chronic aquatic toxicity data are available for all five PBT chemicals. However, data were available for organisms spanning three trophic levels for all the PBT chemicals, except for PCTP.

The hazard summaries relevant to human health focus on repeated-dose studies given the PBT nature of the chemicals of interest. Available published and unpublished repeated-dose toxicity data are tabulated according to health endpoints and the identified studies are briefly summarized. Human health hazard data are presented in the context of existing toxicological assessments, when available.

Available hazard information is tabulated and briefly summarized within this document. The purpose of the environmental and human health summary is to identify known hazards of the PBT chemicals; the information in this document is not meant to represent an exhaustive literature review nor an analysis of relative importance or comparative dose-response among hazards. EPA leveraged previous data compilations and existing information, wherever possible, as the initial data gathering approach and to survey the environmental and human health hazard data and information.

The document is intended to provide an overview of the nature and extent of hazards for use in making risk-based regulatory decisions. However, some qualitative interpretation is provided in discussing the reported data. Similarly, the document summarizes points of departure (e.g., NOAEL/LOAEL) or other hazard benchmarks as reported in the data source, rather than the

'selection' of particular studies for use in conjunction with any particular exposure pathway(s) or risk assessment scenarios, or a dose-response analysis conducted by EPA.

2. Background

Under the Toxic Substances Control Act (TSCA), as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act, EPA has new authorities to regulate existing chemical substances. Section 6(h) of TSCA directs EPA to take expedited regulatory action under section 6(a), for certain PBT chemicals.

The chemical substances subject to TSCA section 6(h) are those:

- Identified in the 2014 update of the TSCA Work Plan for Chemical Assessments;
- That the Administrator has a reasonable basis to conclude are toxic and that with respect to persistence and bioaccumulation, score high for one and either high or moderate for the other, under the 2012 TSCA Work Plan Chemicals Methods Document (or a successor scoring system);
- That, are not a metal or a metal compound;
- For which the Administrator has not completed a Work Plan Problem Formulation, initiated a review under section 5 (new chemicals), or entered into a consent agreement under section 4 (testing), prior to June 22, 2016;
- Exposure to which under the conditions of use is likely to the general population, to a potentially exposed or susceptible subpopulation, or the environment, on the basis of an exposure and use assessment; and
- That are not designated as a high priority substance by EPA and are not the subject of a manufacturer request for a risk evaluation.

Taking the above criteria into account, EPA has identified the following five PBT chemicals for proposed action under TSCA section 6(h):

- Decabromodiphenyl ether (DecaBDE) (CASRN 1163-19-5)
 - Scored high for hazard, high for persistence, and high for bioaccumulation on the 2014 update
- Hexachlorobutadiene (HCBd) (CASRN 87-68-3)
 - Scored high for hazard, high for persistence, and high for bioaccumulation on the 2014 update
- Phenol, isopropylated, phosphate (3:1) (PIP 3:1) (CASRN 68937-41-7)
 - Scored high for hazard, high for persistence, and high for bioaccumulation on the 2014 update
- 2,4,6-Tris(tert-butyl) phenol (2,4,6 TTBP) (CASRN 732-26-3)
 - Scored high for hazard, moderate for persistence, and high for bioaccumulation on the 2014 update

- Pentachlorothiophenol (PCTP) (CASRN 133-49-3)
 - Scored high for hazard, high for persistence, and high for bioaccumulation on the 2014 update

3. Approach for Surveying the Chemical-Specific Hazard Data

The purpose of this document is to identify known hazards of the PBT chemicals; the information in this document is not meant to represent an exhaustive literature review nor an analysis of relative importance or comparative dose-response among hazards. Under TSCA section 6(h), EPA is required to take expedited regulatory action for PBT chemicals meeting the abovementioned criteria.

EPA conducted chemical-specific searches for information on the following five PBT chemicals to conduct a survey of available data: decabromodiphenyl ether (CASRN 1163-19-5), hexachlorobutadiene (CASRN 87-68-3), phenol, isopropylated, phosphate (3:1) (CASRN 68937-41-7), 2,4,6-Tris(tert-butyl) phenol (CASRN 732-26-3), and pentachlorothiophenol (CASRN 133-49-3).

3.1. Environmental Hazard Data

EPA leveraged previous data compilations, wherever possible, as the initial data gathering approach. Literature already available from various governmental jurisdictions were relied on to summarize potential environmental hazards. Database searches from the European Chemicals Agency (ECHA) Database and EPA's ECOTOXicology knowledgebase (ECOTOX) were utilized to identify environmental hazard data for the PBT chemicals. Additionally, EPA searched for chemical assessments conducted by the following sources:

- Environment Canada Health Canada,
- Australian Government Department of Health National Industrial Chemicals Notification and Assessment Scheme (NICNAS),
- Organisation for Economic Co-operation and Development (OECD) Screening Information Dataset (SIDS),
- United Nations Environment Programme (UNEP) Stockholm Convention on Persistent Organic Pollutants, and
- USEPA HPV Chemical Challenge Program.

The above-mentioned databases and sources of chemical assessments did not include data on every chemical. When applicable, literature already gathered from other jurisdiction assessments were relied upon to examine potential environmental hazard. Identified data in these sources are summarized below.

EPA conducted a high-level literature search and leveraged existing information, wherever possible, to facilitate the data gathering effort supporting potential risk management practices. Environmental literature was searched for and screened following well accepted methods,

approaches and procedures established for the ECOTOX knowledge base. The ECOTOX standard operating procedures (SOPs) provide details about the information needs driving the environmental literature searches¹. Due to the lack of data initially identified for 2,4,6-Tris(tert-butyl) phenol and pentachlorothiophenol (PCTP) in the various sources cited above and in ECOTOX, additional searches on the Web of Science and Science Direct were conducted.

For all literature searches, both the chemical name and the CAS registry number (CASRN) were used as key words. There was no date limit used for any of the literature searches. If there was a date limit option included for any of the databases, the whole range was used (i.e., ECOTOX's publication year range is 1915 to 2018).

3.2. Human Health Hazard Data

EPA leveraged previous data compilations and existing information, wherever possible, as the initial data gathering approach and to survey the human health hazard data and information. Using the CASRN for each PBT chemical, EPA searched the International Toxicity Estimates for Risk (ITER; <https://toxnet.nlm.nih.gov/newtoxnet/iter.htm>) database for available human health assessments for the five PBT chemicals. This database searches for assessments was from the following organizations:

- Agency for Toxic Substances and Disease Registry (ATSDR),
- Health Canada,
- The International Agency for Research on Cancer (IARC),
- World Health Organization International Programme on Chemical Safety (IPCS),
- National Science Foundation (NSF) International,
- National Institute for Public Health and the Environment (RIVM),
- Texas Commission on Environmental Quality (TCEQ), and
- U.S. EPA Integrated Risk Information System (IRIS).

In addition, toxicological assessments from California EPA (CalEPA), U.S. EPA Provisional Peer Review Toxicity Values for Superfund (PPRTV), U.S. EPA Alternative Assessments, and the Organisation for Economic Co-operation and Development (OECD) Screening Information Dataset (SIDS) were separately searched for hazard information on the PBT chemicals. Several human health assessments were identified from this search for DecaBDE and HCB. For the remaining three chemicals, EPA searched the European Chemicals Agency (ECHA) database, EPA's ChemView, and the Hazardous Substances Data Bank (HSDB) on TOXNET. The databases were searched by chemical CASRN to gather additional human health data/information from unpublished studies. For PCTP, no relevant repeated dose animal toxicity studies or human data were available for the chemical. Thus, a search was conducted for analogous chemicals that are known to metabolize or degrade into PCTP using the expanded results feature in the HSDB.

¹ECOTOX and related SOPs (<https://cfpub.epa.gov/ecotox/help.cfm?helptabs=tab4>).

The summaries were constructed from the hazards identified in the toxicological assessments, when available. For chemicals without existing assessments, all repeated-dose studies identified in the additional literature searches were provided in the evidence tables and summarized in the text.

The following chapters provide a summary of the hazard data for each of the chemicals subject to TSCA section 6(h) identified using the methods provided in Chapter 3. The hazards are provided as brief summaries and in tables.

4. Decabromodiphenyl Ether

4.1. Environmental Hazard Summary

The available information indicates that DecaBDE is acutely toxic to aquatic invertebrates (daphnia) at concentration as low as 0.02 mg/L ([Nakari and Huhtala, 2010](#)). Acute toxicity to fish varies among species, with acute effects reported in the range of 0.01 to >500 mg/L ([Nakari and Huhtala, 2010](#); [Chemicals Inspection and Testing Institute, 1992](#)). No effect on growth of a sediment invertebrate (midge) was observed up to 5,000 mg/kg sediment dry weight ([Hardy et al., 2012](#)). Chronic exposures of DecaBDE to various species of vertebrates also show the potential to cause both growth and reproductive toxicity as well as an array of other toxicological endpoints (e.g., neurotoxicity, behavioral changes) ([He et al., 2011](#); [Noyes et al., 2011](#); [Kuo et al., 2010](#); [Kierkegaard et al., 1999](#)). Data on the effects of DecaBDE on aquatic vegetation was not identified, however, one study demonstrated that at exposure concentrations up to 1 mg/L, DecaBDE did not inhibit the growth of three species of marine algae ([Walsh et al., 1987](#)). In terms of terrestrial toxicological data on DecaBDE, there are three chronic earthworm studies that have exposures spanning between 14 and 56 days that indicate DecaBDE is toxic at high concentrations ($\geq 2,000$ mg/kg soil dry weight) ([ECHA, 2018a](#); [Hardy et al., 2011](#); [Great Lakes Chemical Corp, 2000](#)). Similarly, with a variety of commonly grown vegetables, even at the highest exposure concentration (5,349 mg/kg soil dry weight), no mortality was documented and there was no reduction in growth ([Wildlife Intl LTD, 2001](#)).

Most of the available hazard information on DecaBDE are for a product containing DecaBDE, therefore it is important to note that many of the studies cited in Table 4-1 examined effects from the exposure to a mixture containing DecaBDE. Commercial mixtures containing DecaBDE (77-98%) also consist of smaller amounts of congeners of nona- and octa-brominated diphenyl ether, although the product composition can vary greatly ([ECHA, 2012](#); [U.S. EPA, 2008](#)).

Table 4-1. Summary of Surveyed Environmental Hazard Data for Decabromodiphenyl Ether

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
Aquatic	Acute	Rainbow trout	96-hr LLR ₅₀ (lethality)	>110	mg/L	Water accommodated fraction (WAF) exposure; nominal	Hardy et al. (2012)
		Zebrafish embryo	<8-d LOAEL (neurological pathway expression and abnormal behavior)	12.5	mg/kg	Sediment to embryo bioavailability test with BDE-209. Positive bioaccumulation of BDE-209.	Garcia-Reyero et al. (2014)^a
		Zebrafish	96-hr LOEC (hatching)	0.0125	mg/L	Non-good laboratory practice (GLP) International Organization for Standardization ((ISO) 12890, 1999); BDE-209 exposure above the water solubility (0.72 µg/L)	Nakari and Huhtala (2010)^a
		Killifish	48-hr LC ₅₀ (lethality)	>500	mg/L	Non-GLP Japanese Industrial Standards ((JIS) K 0102-1986-71); only one concentration (500 mg/L- nominal) used; no information on purity	Chemicals Inspection and Testing Institute (1992)
		Daphnid	48-hr EC ₅₀ (immobilization)	0.019	mg/L	GLP (ISO 6341, 1997); BDE-209 exposure above the water solubility (0.72 µg/L)	Nakari and Huhtala (2010)^a
		Algae	96-hr EC ₅₀ (growth)	>1	mg/L	Only 0 and 1 mg/L exposures	Walsh et al. (1987)
	Chronic	Rainbow trout	120-d LOAEL (uptake)	>10	mg/kg bw/d	Non-GLP 49-d feeding study with 71-d depuration; Dow FR-300-BA	Kierkegaard et al. (1999)

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
		Lake whitefish	30-d LOAEL (growth)	2	µg/g food	BDE-209	Kuo et al. (2010)^a
		Zebrafish	LOAEL (delayed hatching, reduction in motor neuron development and growth)	0.001-1	µM	Multigenerational exposure to BDE-209 (exposure period n/a).	He et al. (2011)^a
		Fathead minnow	28-d LOAEL (thyroid hormone regulation)	9.8	µg/g food	Followed by 14-d depuration; BDE-209	Noyes et al. (2011)^a
		Goldfish	21-d LOEC (oxidative stress)	10	mg/kg bw	Intraperitoneal exposure	Feng et al. (2013)
		African clawed frog	45-d LOEC (thyroid system disruption; growth)	1; 1000	ng/L	BDE-83R	Qin et al. (2010)^a
		Midge	28-d LOEC (growth)	>5,000	mg/kg sediment dw	GLP	Hardy et al. (2012)
Terrestrial	Chronic	Earthworm	14-d LOEL (body chemistry changes)	2000	µg/cm ²	n/a	Great Lakes Chemical Corp (2000)
		Earthworm	28-d LOEC (mortality and reproduction)	NOEC: 1,910; LOEC: 3,720	mg/kg soil dw	Organisation for Economic Co-operation and Development (OECD) GLP study (OECD TG-222)	Hardy et al. (2011)

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
		Earthworm	56-d EC ₅₀ (survival and reproduction)	>4910	mg/kg soil dw	GLP (EPA OPPTS 850.6200; OECD 207); equal proportions of three different products	ECHA (2018a) ; (unnamed 2001 and 2002 report) ^a
		Onion, Cucumber, Soybean, Ryegrass, Tomatoes and Corn	21-d NOEC (growth)	5349; >6250 (nominal)	mg/kg soil dw	GLP (OECD 208; EPA OPPTS 850.4100; EPA OPPTS 850.4225); equal proportions of three different products	Wildlife Intl LTD (2001) ^a

^aUse of a commercial product or mixture (containing the target chemical) in the study.

4.2. Human Health Hazard Summary

Toxicological assessments have been conducted by EPA's IRIS program ([U.S. EPA, 2008](#)), Health Canada ([Health Canada, 2012](#)), ATSDR, and IARC ([IARC, 1999a](#)). Oral repeated dose animal data for DecaBDE indicate developmental neurological effects, developmental immunological effects, general developmental toxicity, and liver effects.

Several published oral studies have been conducted and range from short-term developmental studies to 2-year carcinogenicity studies in rats and mice (Table 4-2). Limited information is available on the effects from inhalation and dermal routes of exposure so no conclusion was made regarding these exposure routes. The available toxicological assessments identified developmental neurotoxicity in several developmental studies with dose-related effects such as altered behavior, reduced strength and reflexes, reduced locomotor activity, and impaired learning ([Health Canada, 2012](#); [U.S. EPA, 2008](#)). Dose-related brain effects were reported in adult rats as well, which was demonstrated by a decrease in brain weight following 28-days of oral gavage ([Van der Ven et al., 2008](#)).

Developmental immunotoxicity was indicated by reduced IgM levels and reduced natural killer cell numbers in F1 female mice that were dose-related ([Teshima et al., 2008](#)). The toxicological assessment also found that general developmental effects were also observed in mice as indicated by reduced DNA integrity in the sperm and reduced serum T3 levels ([Tseng et al., 2013](#); [Tseng et al., 2008](#); [Hsu et al., 2006](#)) and increased liver weights, centrilobular hypertrophy and increased cytoplasmic eosinophilia in renal proximal tubules in rat pups ([Fujimoto et al., 2011](#)). Noncancer liver effects were observed in a 2-year dietary study in rats which reported degeneration and thrombosis in the liver ([NTP, 1986](#)).

In addition, animal data indicates that there is suggestive evidence for carcinogenic potential based on increased liver granulomas, centrilobular hypertrophy, and adenomas and carcinomas as well as increased thyroid follicular cell hyperplasia in mice ([NTP, 1986](#)). NOAELs for developmental effects ranged from 1.34 mg/kg-day to 10 mg/kg-day in mice and rats. The cancer slope factor for liver neoplasms and carcinomas is 7×10^{-4} per mg/kg-day ([U.S. EPA, 2008](#)).

Table 4-2. Summary of Surveyed Human Health Hazard Data for Decabromodiphenyl Ether

Organ/System	Study Type	Doses	POD	Health Effect	Reference
Developmental neurotoxicity	Neurodevelopmental oral study to neonatal mice	0, 1.34, 2.22, 13.4, 20.1 mg/kg-day	NOAEL: 1.34 mg/kg-day LOAEL: 2.22 mg/kg-day	Change in behavior, decreased activity, poor habituation	Johansson et al. (2008)
Developmental neurotoxicity	Oral gavage study in pregnant mice from PND 2-15	0, 6, 20 mg/kg-day	LOAEL: 6 mg/kg-day	Effects on palpebral reflex, grip strength, locomotor activity, struggling behavior in F1 pups	Rice et al. (2007)
Developmental neurotoxicity	Oral gavage study in pregnant mice from PNDs 2-15	0, 6, 20 mg/kg-day	NOAEL: 6 mg/kg-day LOAEL: 20 mg/kg-day	Altered performance in neurological and visual tests suggesting impaired learning in F1 offspring	Rice et al. (2009)
Developmental neurotoxicity	OECD TG 426; Oral study in pregnant rats from GD 6 to lactation day 21	0, 1, 10, 100, 1000 mg/kg-day	NOAEL: 10 mg/kg-day LOAEL: 100 mg/kg-day	Increase in pup deaths, reduced motor activity	Bieseimer et al. (2011)
Developmental neurotoxicity	Single dose gavage in Sprague-Dawley male rats on PND 3	0, 6.7, 20.1 mg/kg-day	NOAEL: none identified LOAEL: 6.7 mg/kg-day	Changes in locomotion, activity, and rearing	Viberg et al. (2007)
Developmental neurotoxicity	Single dose gavage in NMRL male mice on PND 3 and 19	0, 2.22, 20.1 mg/kg-day	NOAEL: 2.22 mg/kg-day LOAEL: 20.1 mg/kg-day	Changes in locomotion, activity, and rearing	Viberg et al. (2003)
Developmental immunotoxicity	Oral gavage of mice dams from day 10 of gestation to PND 21	0, 10, 100, 1000 ppm	NOAEL: not reported LOAEL: 5 mg/kg-day	Reduced IgM and reduced NK cell counts in F1 females	Teshima et al. (2008)
Developmental	Oral gavage of mice dams on days 0-17 of pregnancy	0, 10, 500, 1500 mg/kg-day	LOAEL: 10 mg/kg-day	Reduced sperm DNA integrity, decrease T3, and sperm H ₂ O ₂ in F1 males,	(2013) ; Tseng et al. (2008) ; Hsu et al. (2006)
Developmental	Oral dietary study in pregnant rats from GD 10 to PND 20	0, 10, 100, 1000 ppm	LOAEL: 0.7-2.4 mg/kg-day	Liver and kidney histopathological effects in F1 pups	Fujimoto et al. (2011)
Oxidative stress	60-day oral gavage mouse study	0, 0.1, 40, 80, 160 mg/kg-day	NOAEL: 0.1 mg/kg-day LOAEL: 40 mg/kg-day	Decreased superoxide dismutase; increased malonyldialdehyde	Liang et al. (2010)

Organ/System	Study Type	Doses	POD	Health Effect	Reference
Brain	28-day oral gavage Wistar rat study	0, 1.87, 3.75, 7.5, 15, 30, 60 mg/kg-day	NOAEL: 30 mg/kg-day LOAEL: 60 mg/kg-day	Decreased brain weight	Van der Ven et al. (2008)
Liver	2-year dietary study in F344 rats	Males: 0, 1120, 2240 mg/kg-day	NOAEL: 1120 mg/kg-day in males LOAEL: 2240 mg/kg-day in females	Degeneration and thrombosis of the liver	NTP (1986)
Liver	2-year dietary study in B6C3F1 mice	Males: 0, 3200, 6650 mg/kg-day	NOAEL: none identified LOAEL: 3200 mg/kg-day	Increased granulomas, hypertrophy, adenomas and carcinomas in the liver	NTP (1986)
Thyroid	2-year dietary study in B6C3F1 mice	Males: 0, 3200, 6650 mg/kg-day	NOAEL: none identified LOAEL: 3200 mg/kg-day	Increased follicular cell hyperplasia	NTP (1986)

5. Hexachlorobutadiene

5.1. Environmental Hazard Summary

HCBD is acutely toxic to aquatic invertebrates at concentrations ranging from 0.032 to 0.5 mg/L ([Knie et al., 1983](#); [U.S. EPA, 1980](#)). Acute LC_{50s} in two species of fish were both 0.09 mg/L ([Geiger et al., 1985](#); [Leeuwangh et al., 1975](#)). Algae appear to be less sensitive to HCBD, as compared to aquatic invertebrates and fish, with a reported NOAEL of 25 mg/L ([Bringmann and Kuhn, 1977](#)). There is only chronic HCBD aquatic toxicity data available for fish. HCBD is toxic to fish at exposure levels ranging from 0.0096 to 0.16 mg/L, where the effects ranges from reductions in growth, increases in mortality, and liver damage ([Hermens et al., 1985](#); [Benoit et al., 1982](#); [Laseter et al., 1976](#)). HCBD is both acutely and chronically toxic to aquatic life at very low concentrations. A single toxicity test was identified for terrestrial organisms. A 90-d chronic exposure of HCBD to quail revealed a significant reduction in chick survival when parents were fed 10 mg HCBD/kg food-day ([Schwetz et al., 1974](#)).

EPA used information from toxicological assessments of hexachlorobutadiene (HCBD) from Health Canada, data from the ECHA database, data from ECOTOX. As seen in Table 5-1, all surveyed data except for one study focuses on the aquatic toxicological effects of HCBD.

Table 5-1. Summary of Surveyed Environmental Hazard Data for Hexachlorobutadiene

Media	Study duration	Organism	Endpoint	Hazard value	Unit	Chemical and Study Specification	Reference
Aquatic	Acute	Fathead minnow	96-hr LC ₅₀ (lethality)	0.09	mg/L	n/a	Geiger et al. (1985)
		Goldfish	96-hr LC ₅₀ (lethality)	90	µg/L	n/a	Leeuwangh et al. (1975)
		Mysid shrimp	96-hr LC ₅₀ (lethality)	32	µg/L	n/a	U.S. EPA (1980)
		Sowbug	96-hr LC ₅₀ (lethality)	130	µg/L	n/a	Leeuwangh et al. (1975)
		Daphnia	24-hr EC ₅₀ (endpoint n/a)	0.5	mg/L	n/a	Knie et al. (1983)
		Algae	8-d NOAEL	25	mg/L	exposure concentration over water solubility	Bringmann and Kuhn (1977)
	Chronic	Fathead minnow	28-d LOAEL (lethality and growth)	0.013	mg/L	n/a	Benoit et al. (1982)
		Guppy	14-d LC ₅₀ (lethality)	0.16	mg/L	n/a	Hermens et al. (1985)
		Goldfish	49-d LOAEL (body weight; liver weight and erratic behavior)	0.0096; 0.03	mg/L	n/a	Leeuwangh et al. (1975)
		Largemouth bass	10-d LOAEL (kidney and liver damage)	0.03195	mg/L	n/a	Laseter et al. (1976)
Terrestrial	Chronic	Quail	90-d LOAEL (chick survival)	10	mg/kg food	n/a	Schwetz et al. (1974)

5.2. Human Health Hazard Summary

Toxicological assessments have been conducted by California EPA ([Rabovsky, 2000](#)), EPA's PPRTV ([U.S. EPA, 2007](#)) and IRIS ([U.S. EPA, 1988](#)) programs, Health Canada ([Health Canada, 2012](#)), the International Agency for Research on Cancer ([IARC, 1999b](#)) and the Agency for Toxic Substances and Disease Registry ([ATSDR, 1994](#)). Inhalation and oral animal data for HCBd indicate renal, reproductive, and developmental effects.

Numerous published oral studies ranging from 2 weeks to 2 years in rats and mice demonstrated renal effects (Table 5-2). The available toxicological assessments found that dose-related increases in histopathological lesions in the kidneys were observed such as renal tubule regeneration, degeneration of the renal tubules corresponding to biochemical changes in the urine, and kidney weight increases ([U.S. EPA, 2007](#)). Renal adenomas and carcinomas were observed after 2 years and HCBd was considered to be a possible human carcinogen ([U.S. EPA, 1988](#)).

Reproductive effects were observed in an inhalation developmental study in rats and was characterized by reduced body weight gains in maternal adults ([Saillenfait et al., 1989](#)). Developmental effects characterized by reduced fetal body weights in the F1 generation were observed following either oral or inhalation exposures in rats ([Field et al., 1990](#); [Saillenfait et al., 1989](#); [Harleman and Seinen, 1979](#)). NOAELs for kidney effects ranged from 0.2 to 10 mg/kg-d for oral exposures. LOAELs for developmental effects ranged from 0.5 mg/kg-day to 11 mg/kg-day for oral exposures and inhalation exposures for reproductive and developmental effects yielded NOAECs between 2 and 10 ppm.

Table 5-2. Summary of Surveyed Human Hazard Data for Hexachlorobutadiene

Organ/System	Study type	Doses	POD	Health Effect	Reference
Kidney	Oral dietary study for 4 weeks in male and female Wistar rats	0, 25, 100, 400 ppm	NOAEL: 25 ppm (2.6 mg/kg-day) LOAEL: 100 ppm (10.2 mg/kg-day)	Increased kidney weights, histopathological effects, blood and urine biochemistry effects	Jonker et al. (1993)
Kidney	13-week oral dietary study in male and female B6C3F1 mice	0, 1, 3, 10, 30, 100 ppm	NOAEL: 1 ppm (0.2 mg/kg-d) LOAEL: 3 ppm (0.5 mg/kg-d)	Increased renal tubule regeneration	NTP (1991) ; Yang R et al. (1989)
Kidney	Oral gavage study for 21 consecutive days in male Sprague-Dawley rats	0, 0.2, 20 mg/kg-day	NOAEL: 0.2 mg/kg-day LOAEL: 20 mg/kg-day	Increased DNA repair in kidneys and increased kidney weights	Stott et al. (1981)
Kidney	Oral dietary study for 2 weeks in Wistar rats	0, 50, 150, 450 ppm	LOAEL: 50 ppm (8 mg/kg-day)	Degeneration of renal tubules	Harleman and Seinen (1979)
Kidney	Oral developmental study in female Wistar rats for 18 weeks	0, 150, 1500 ppm	LOAEL: 150 ppm (11 mg/kg-day)	Decreased body weight gain, increased kidney weights, and altered kidney histopathology in F0 dams	Harleman and Seinen (1979)
Kidney	Oral 13-week study in male and female Wistar rats	0, 0.4, 1.0, 2.5, 6.3, 15.6 mg/kg-day	NOAEL: 1.0 mg/kg-day LOAEL: 2.5 mg/kg-day	Histopathological effects in kidneys	Harleman and Seinen (1979)
Kidney	Oral 2-year dietary study in male and female Sprague-Dawley rats	0, 0.2, 2, 20 mg/kg-day	NOAEL: 0.2 mg/kg-day LOAEL: 2 mg/kg-day	Kidney histopathological lesions, changes in urine biochemistry	Kociba et al. (1977)
Kidney	Oral 2-year dietary study in male and female Sprague-Dawley rats	0, 0.2, 2, 20 mg/kg-day	Oral slope factor: 7.8×10^{-2} mg/kg-day; Inhalation unit risk: 2.2×10^{-5} mg/kg-day	Increased renal tubular adenomas and carcinomas	Kociba et al. (1977) ; U.S. EPA (1987)
Kidney	Oral dietary developmental study through lactation in male and female Sprague-Dawley rats	0, 0.2, 2, 20 mg/kg-day	NOAEL: 0.2 mg/kg-day LOAEL: 2 mg/kg-day	Kidney histopathological lesions in F0 adults	Schwetz et al. (1977)
Kidney	Oral 30 dietary study in female Sprague-Dawley rats	0, 1, 3, 10, 30, 65, 100 mg/kg-day	NOAEL: 10 mg/kg-day LOAEL: 30 mg/kg-day	Increase in renal lesions	Kociba et al. (1977)

Organ/System	Study type	Doses	POD	Health Effect	Reference
Developmental	Oral dietary developmental study in pregnant CD rats through PND 10	0, 100, 200, 400, 750, 1100, 1500 ppm	NOAEL: 200 ppm (22.5 mg/kg-day) LOAEL: 400 ppm (35.3 mg/kg-day)	Reduced pup body weight and increased kidney weights in F1	Field et al. (1990)
Developmental	Inhalation developmental toxicity study in Sprague-Dawley rats to PND 21	0, 2, 5, 10, 15 ppm	NOAEC: 10 ppm LOAEC: 15 ppm	Reduced fetal body weight in F1	Saillenfait et al. (1989)
Developmental	Oral developmental study in female Wistar rats for 18 weeks	0, 150, 1500 ppm	LOAEL: 150 ppm (11 mg/kg-day)	Decreased fetal body weight in F1 generation	Harleman and Seinen (1979)
Reproductive	Inhalation developmental toxicity study in Sprague-Dawley rats to PND 21	0, 2, 5, 10, 15 ppm	NOAEC: 2 ppm LOAEC: 5 ppm	Reduced maternal weight gain in F0 adults	Saillenfait et al. (1989)

6. Phenol, isopropylated, phosphate (3:1)

6.1. Environmental Hazard Summary

The CASRN 68937-41-7 does not represent a discrete chemical, thereby making it difficult to know the degree of propylation that results in the hazardous effects summarized in Table 6-1. Most of the studies cited in Table 6-1 represent exposures to whole commercial products and the amount of PIP (3:1) varies greatly in content and propylation configurations; the exposure to other chemicals within the product (e.g., triphenyl phosphate) may have influenced the effects observed.

The majority of the toxicity tests where PIP (3:1) is evaluated used whole product mixtures, and if reported, the table provides the percentage of PIP (3:1) present in the tested product. Acute toxicity tests with a variety of products or formulations, most also containing 5% triphenyl phosphate, indicate acute toxicity (96-hr LC50s) ranging from 1.6 in rainbow trout to >1000 mg/L in zebrafish ([ECHA, 2018b](#); [U.S. EPA, 2010](#)). Similarly, 5% triphenyl phosphate preparations were acutely toxic to daphnids over a range from 0.83 to >100 mg/L ([ECHA, 2018b](#); [U.S. EPA, 2012](#)). The algal toxicity tests available do not provide a threshold for toxicity, but the exposure concentrations used in the studies suggest that PIP (3:1) is not acutely toxic to algae at concentrations below 1,000 mg/L ([ECHA, 2018b](#)). Fathead minnows chronically exposed to Kronitex 200 and Reofos 35, two products containing PIP (3:1), as well as triphenyl phosphate which is aquatically toxic, resulted NOECs of 0.088 and 0.0031 mg/L, respectively ([ECHA, 2018b](#)). Daphnids and chironomids (sediment exposure) chronically exposed to the commercial product Reofos 35 for 21 and 28 days, respectively, showed toxicity, with LOECs of 106 µg/L, and 37 mg/kg sediment dry weight, respectively ([ECHA, 2018b](#)). At the highest concentration tested, the commercial product 310M did not have effect on various vegetables (e.g., wheat, radish, mung bean) ([ECHA, 2018b](#)). The 14-d NOEC for growth in earthworms exposed to the commercial product Reofos was 500 mg/kg soil dry weight, whereas the 56-day NOEC for reproduction was 250 mg/kg soil dry weight ([ECHA, 2018a](#)).

Table 6-1. Summary of Surveyed Environmental Hazard Data for Phenol, Isopropylated, Phosphate (3:1)

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
Aquatic	Acute	Fathead minnow	96-hr LC ₅₀ (lethality); LOEC; NOEC (hemorrhaging, and abnormal surfacing behavior)	10.8; 5.6; 3.2	mg/L	Non-GLP; Triphenyl phosphate >5%	ECHA (2018b) ; (unnamed 1978 report)
		Fathead minnow	96-hr LC ₅₀ (lethality)	50.1	mg/L	Non-GLP; Kronitex 200 (Triphenyl phosphate >5%)	ECHA (2018b) ; (unnamed 1978 report) ^a
		Zebrafish	96-hr NOEC	>1000	mg/L	GLP (OECD 203); Durad 310M (Triphenyl phosphate <5%)	ECHA (2018b) ; (unnamed 1997 report) ^a
		Rainbow trout	96-hr LC ₅₀ (lethality); LOEC (twitching behavior and labored respiration)	1.6; 1	mg/L	Non-GLP; Triphenyl phosphate >5%	U.S. EPA (2010) ; ECHA (2018b) (unnamed 1979 report)
		Rainbow trout	96-hr LC ₅₀ ; NOEC (mortality)	4.46; < 0.56	mg/L	Non-GLP; Kronitex 200 (Triphenyl phosphate >5%)	ECHA (2018b) ; (unnamed 1979 report) ^a
		Daphnid	48-hr LC ₅₀ ; NOEC (lethality)	1.5; 1.0	mg/L	Non-GLP; Kronitex 200 (Triphenyl phosphate >5%)	ECHA (2018b) ; named 1979 report) ^a
		Daphnid	48-hr NOEC (immobilization)	>1000	mg/L	GLP (OECD 202-immobilization); Curad 310M; prepared as WAFs	ECHA (2018b) ; (unnamed 2001 report) ^a
		Daphnid	48-hr LC ₅₀ (lethality)	2.44	mg/L	non-GLP; Triphenyl phosphate >5%	ECHA (2018b) ; (unnamed 1979 report) ^a
		Daphnid	48-hr EC ₅₀ (immobilization)	0.83	mg/L	n/a	U.S. EPA (2012) (not referenced)
Algae	96-hr EC ₅₀ (growth)	>2.5	mg/L	GLP (OECD 201; OPPTS 850.5400; EU Method C.3); Reofos 65 (Triphenyl phosphate >5%)	ECHA (2018b) ; (unnamed 2005 report) ^a		

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
		Algae	72-hr EC ₅₀ (growth)	>1000	mg/L	GLP (OECD 201); Durad 310M. Prepared as WAF (Triphenyl phosphate <5%)	ECHA (2018b) ; (unnamed 2001 report) ^a
	Chronic	Fathead minnow	33-d NOEC; LOEC (growth and development abnormalities)	3.1; 8.2	µg/L; mg/L	GLP (OECD 210; EPA OPPTS 850.1400); Reofos 35	ECHA (2018b) ; (unnamed 2014 report) ^a
		Fathead minnow	90-d NOEC	0.088 (Kronitex 200); 0.029 (Phosflex 31P)	mg/L	Non-GLP; Kronitex 200 (four to six per cent triphenyl phosphate, seven to 10 per cent 2-isopropylphenyl diphenyl phosphate, 20-25 per cent 4-isopropylphenyl diphenyl phosphate, along with bis-(2-isopropylphenyl) phenyl phosphate and minor amounts of di-, tri- and tetraisopropyl-substituted triphenyl phosphates) or Phosflex 31P (28-30 per cent triphenyl phosphate, along with isomers of isopropylphenyl diphenyl phosphate, isomers of diisopropylphenyl diphenyl phosphate and tri-substituted phenol phosphates. The study was carried out using a flow-through test system). Effects based on growth (just Kronitex) and mortality (Phosflex- both endpoints).	ECHA (2018b) ; (unnamed 1986 report) ^a

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
		Daphnid	21-d NOEC; LOEC (growth, reproduction)	41.5; 106;	µg/L	GLP (OECD 211; EPA OPPT 850.1300); Reofos 35	ECHA (2018b) ; (unnamed 2014 report) ^a
		Chironomid	28-d EC50 (emergence); LOEC (developmental rate); NOEC	87; 37; <37	mg/kg sediment dw	GLP (OECD 218; ASTM E 1706-05). EC50 (emergence rate); LOEC (development rate); NOEC (development rate); Reofos 35	ECHA (2018b) ; (unnamed 2015 report) ^a
		Algae	14-d LOEC (growth)	0.1	mg/L	Phosflex 31P (Triphenyl phosphate 28-30%)	Sanders et al. (1985)
Terrestrial	Sub-chronic	Earthworm	14-d NOEC (growth)	500	mg/kg soil dw	GLP (OECD 207); Reofos 35	ECHA (2018b) (unnamed 2014 report) ^a
		Wheat, radish, mung bean	19; 18; 19-d EC50 (seedling emergence)	>100	mg/kg soil dw	GLP (OECD 208); Durad 310M	ECHA (2018b) (unnamed 2001 report) ^a
	Chronic	Earthworm	56-d NOEC (reproduction)	250	mg/kg soil dw	GLP (OECD 222; ISO 11268-2); Reofos 35	ECHA (2018a) (unnamed 2017 report) ^a

^aUse of a commercial product or mixture (containing CAS# 68937-41-7) in the study.

6.2. Human Health Hazard Summary

Surveyed inhalation and oral animal data for Isopropylated, phosphate (3:1) indicate reproductive and developmental effects, increased mortality, neurological effects and effects on systemic organs, specifically adrenals, liver, ovary, heart, and lungs ([U.S. EPA, 2015](#)). All available repeated-dose studies were unpublished study reports available on the ECHA database for various molecular compositions of isopropylated phenol phosphate (Table 6-2).

An OECD 422 guideline oral gavage study in Sprague-Dawley rats reported dose-dependently reduced copulation and reduced conception indices ([ECHA, 2018a](#)). In addition, postnatal survival and early postnatal development were reduced in this study. Various systemic organ effects were noted by increased ovarian, adrenal, and liver weights with reduced epididymal weights in the parental generation.

A 90-day oral gavage OECD 408 guideline study observed dose-dependently increased adrenal weights with corresponding macroscopic changes in both male and female rats as well as increased liver weights with centrilobular or pablobular hypertrophy, increased ovary weights with interstitial cell vacuolation, and increased thyroid weights with follicular cell hypertrophy ([ECHA, 2018b](#)).

A 90-day inhalation study in Fischer rats, golden hamsters, and rabbits found that all rabbits died in the highest dose group while the exposed rats were reported to have inflammation in the heart and lung and hypertrophy in the ovaries. Finally, hens orally gavaged for 91 days had increased ataxia and correlating neural degenerative changes ([ECHA, 2018a](#)). Altogether, the surveyed data indicate evidence for systemic effects on several organs, reproductive, developmental and neurological effects. The NOAEL for reproductive and developmental effects was 25 mg/kg-d for oral exposures. LOAELs for reproductive and developmental effects were 100 mg/kg-day for oral exposures. Systemic and neurological effect LOAELs were 25-100 mg/kg-day. An inhalation NOAEC of 10 mg/m³ and LOAEC of 100 mg/m³ was identified for systemic effects.

Table 6-2. Summary of Surveyed Human Health Hazard Data for Phenol, Isopropylated, Phosphate (3:1)

Organ/System	Study type	Doses	POD	Health Effect	Reference
Adrenals	90-day oral gavage toxicity study in Sprague-Dawley rats (OECD 408)	0, 25, 100, 325 mg/kg-day	NOAEL: none identified LOAEL: 25 mg/kg-d	Macroscopic effects and increased organ weights	ECHA (2018b)
Systemic organs	90-day oral gavage toxicity study in Sprague-Dawley rats (OECD 408)	0, 25, 100, 325 mg/kg-day	NOAEL: 25 mg/kg-d LOAEL: 100 mg/kg-d	Liver, thyroid and ovary weight increases with corresponding pathology	ECHA (2018b)
Systemic organs	OECD 422 oral gavage study in Sprague-Dawley rats	0, 25, 100, 400 mg/kg-day	NOAEL: not identified LOAEL: 25 mg/kg-day	Increased ovary/oviduct, adrenal glands, and liver weights; decreased epididymal weights in F0	ECHA (2018b)
Reproductive	OECD 422 oral gavage study in Sprague-Dawley rats	0, 25, 100, 400 mg/kg-day	NOAEL: 25 mg/kg/day LOAEL: 100 mg/kg-day	Reduced copulation/conception indices in F0	ECHA (2018b)
Developmental	OECD 422 oral gavage study in Sprague-Dawley rats	0, 25, 100, 400 mg/kg-day	NOAEL: 25 mg/kg/day LOAEL: 100 mg/kg-day	Postnatal development affected in F1	ECHA (2018b)
Mortality, Systemic	90-day inhalation study in Fischer 344 rats, Golden hamsters, and rabbits	0, 10, 100 mg/m ³	NOAEC: 10 mg/m ³ LOAEC: 100 mg/m ³	All rabbits died in high dose group; pulmonary and heart inflammation, ovarian hypertrophy in rats	ECHA (2018b)
Neurological	91-evday oral gavage study in hens	0, 10, 20, 90, 270 mg/kg/day	NOAEL: 20 mg/kg/day LOAEL: 90 mg/kg-day	Ataxia and neural degeneration	ECHA (2018a)

7. 2,4,6-Tris(tert-butyl) phenol

7.1. Environmental Hazard Summary

The information in Table 7-1 demonstrates that 2,4,6-Tris(tert-butyl) phenol (2,4,6 TTBP) is acutely toxic to fish and algae at exposure concentrations as low as 0.061 and 0.04 mg/L, respectively ([ECHA, 2018a](#); [Geiger et al., 1990](#)). Fathead minnows exposed to 0.061 mg/L also experienced significant mortality during a 31-day depuration period ([Geiger et al., 1990](#)). Although the acute daphnid exposure did not result in any effects at the highest exposure concentration tested (0.072 mg/L), a chronic exposure to 2,4,6 TTBP resulted in a EC₅₀ of 2.2 mg/L ([ECHA, 2018a](#)). Unfortunately, there are no further details on the chronic daphnid exposure due to the lack of detail from a summary of the Japanese report. The data presented in Table 7-1 suggests that 2,4,6 TTBP is both acutely and chronically toxic to aquatic organisms. No toxicity data for terrestrial species were identified.

Table 7-1. Summary of Surveyed Environmental Hazard Data for 2,4,6-Tris(tert-butyl) phenol

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
Aquatic	Acute	Carp	96-hr LC ₅₀ (lethality)	>0.048	mg/L	GLP (OECD 203; EU Method C1). Exposures prepared as water soluble fraction (WSF).	ECHA (2018a) ; (unnamed 2015 report)
		Rainbow trout	96-hr LC ₅₀ (lethality)	>0.1	mg/L	GLP (OECD 203)	ECHA (2018a) ; (unnamed 1992 report)
		Fathead minnow	96-hr LC ₅₀ (lethality)	0.061	mg/L	97% purity; exposure to only one concentration (60.9 µg/L)	Geiger et al. (1990)
		Daphnid	48-hr EC ₅₀ (immobilization)	>0.072	mg/L	GLP (OECD 202; EU C2). Exposure prepared as WSF. Effect based on mobility.	ECHA (2018a) ; (unnamed 2015 report)
		Algae	72-hr NOEC	0.04	mg/L	GLP (OECD 201; EU C3). Exposure prepared as WSF. Effect based on growth	ECHA (2018a) ; (unnamed 2015 report)
	Chronic	Fathead minnow	96-hr post-exposure/depuration mortality	0.061	mg/L	97% purity; fish depurated for 31 days after 96-hr exposure	Geiger et al. (1990)
		Daphnid	21-d EC ₅₀ ; NOEC	2.2; 0.36	mg/L	GLP (OECD 221)	ECHA (2018a) ; (Japanese report not referenced)

7.2. Human Health Hazard Summary

Surveyed animal data for 2,4,6-Tris(tert-butyl) phenol (2,4,6 TTBP) indicate liver and developmental effects based on oral animal studies. No inhalation data were identified. Repeated dose studies are limited to two OECD 422 guideline studies in Wistar rats and a 2-year oral carcinogenicity study in Wistar rats (Table 7-2).

Maternal liver weights were dose-dependently increased in one of the OECD 422 guideline studies and was accompanied with hepatocellular hypertrophy and necrosis ([ECHA, 2018a](#)). A two-year oral carcinogenicity study observed increased liver weights, focal necrosis, and corresponding changes in blood biochemistry that were dose-related which is indicative of liver effects in both male and female rats with more severe effects occurring in females ([Matsumoto et al., 1991](#)). One unpublished OECD 422 guideline study report observed reduced body weights in the offspring and increased postnatal ([ECHA, 2018a](#)). Another unpublished OECD 422 guideline study observed reduced pup viability index and reduced weight gain ([ECHA, 2018a](#)). The LOAEL for the observed effects were 10-750 mg/kg-day and the reported NOAELs were 3-150 mg/kg-day.

Table 7-2. Summary of Surveyed Human Health Hazard Data for 2,4,6-Tris(tert-butyl) phenol

Organ/System	Study Type	Doses	POD	Health Effect	Reference
Liver	OECD 422 in Wistar Rats Males: 29 days Females: 41-56 days	0, 3, 10, 30 mg/kg-day	NOAEL: 3 mg/kg-d LOAEL: 10 mg/kg-d	Increased liver weights; Hepatocellular hypertrophy with necrosis in females	ECHA (2018a)
Liver	2-year oral carcinogenicity study in Wistar rats	0, 30, 100, 300, 1000 ppm	NOAEL: 30 ppm (approx. 5 mg/kg-d) LOAEL: 100ppm (approx. 15 mg/kg-d)	Increased liver weights and blood biochemistry; focal necrosis	Matsumoto et al. (1991)
Developmental	OECD 422 in Wistar Rats Males: 29 days Females: 41-56 days	0, 3, 10, 30 mg/kg-day	NOAEL: 3 mg/kg-d LOAEL: 10 mg/kg-d	Reduced pup body weight and increased postnatal loss	ECHA (2018a)
Developmental	OECD 422 in Wistar rats Males: 43 days Females: up to PND 4	0, 30, 150, 750 mg/kg-d	NOAEL: 150 mg/kg-d LOAEL: 750 mg/kg-d	Reduced pup viability	ECHA (2018a)

8. Pentachlorothiophenol

8.1. Environmental Hazard Summary

Pentachlorothiophenol (PCTP) is acutely toxic to aquatic organisms, where mortality was observed in zebrafish and protozoa exposed to 2.8 and 3.1 mg/L, respectively ([U.S. EPA, 2018](#); [HSDB, 2015](#)). Terrestrial toxicity data is limited for PCTP, but 50% mortality was observed within 24 hours when chicken eggs were injected with 1 mg/egg ([U.S. EPA, 2018](#)).

Aquatic and terrestrial plant data are available for PCTP. Radishes and sudangrass exposed to PCTP resulted in a 5-day and 6-day EC₅₀ of 0.762 and 0.479 mM, respectively ([Sund and Nomura, 1963](#)). A study with giant kelp was available but missing details. Two studies listed in Table 8-1 ([CalEPA, 1964](#); [Sund and Nomura, 1963](#)) are not yet available on the public version of ECOTOX but should be available soon.

Table 8-1. Summary of Surveyed Environmental Hazard Data for Pentachlorothiophenol (PCTP)

Media	Study Duration	Organism	Endpoint	Hazard Value	Unit	Chemical and Study Specification	Reference
Aquatic	Acute	Zebrafish	96-hr LC ₁₀₀ (lethality)	2.8	mg/L	mortality	IUCLID HSDB (2015)
	N/A	Golden orfe	LC ₁₀₀ (lethality)	1	mg/L	unknown: study duration; 88% PCTP (2% tetrachlorodithiol, and pentachlorophenol, and 10% pentachlorobenzoldisulfide)	IUCLID HSDB (2015)
	Acute	Giant kelp	4-d (endpoint n/a)	10,000	µg/L	n/a	CalEPA (1964)
	Acute	Ciliate Protozoa (growth)	48-hr EC ₅₀ ; LC ₅₀ (lethality)	4.8; 3.1	Al mg/L	100% purity; no doses reported	ECOTOX U.S. EPA (2018)
Terrestrial	Acute	Chicken	24-hr LC ₅₀ (lethality)	1	mg/egg	100% purity; injection: 0, 1, or 5 mg/egg)	ECOTOX U.S. EPA (2018)
		Radish; Sudangrass	5-d EC ₅₀ ; 6-d EC ₅₀ (growth)	0.000762; 0.000479	M	n/a	Sund and Nomura (1963)

8.2. Human Health Hazard Summary

PCPT is both a metabolite and biodegradation product of pentachloronitrobenzene (PCNB) ([Khan et al., 2011](#)) and a metabolite of hexachlorobenzene ([WHO, 1997](#)). EPA has completed IRIS toxicological reviews for both parent compounds (pentachloronitrobenzene and hexachlorobenzene) and identified liver and reproductive effects associated exposure to the analogous chemicals Table 8-2. No repeat dose animal or human epidemiological data were identified in the surveyed literature for pentachlorothiophenol (PCPT).

A two-year dietary study in dogs found that pentachloronitrobenzene increased liver weight, elevated serum biochemistry levels associated with liver dysfunction and induced cholestatic hepatitis with secondary bile nephrosis ([U.S. EPA, 1987](#)).

A two-year feeding study in Sprague-Dawley rats reported that hexachlorobenzene exposure increased hepatic centrilobular basophilic chromogenesis and increased pup loss ([U.S. EPA, 1988](#)). The NOAEL range for the observed effects ranged from 0.08- 0.29 mg/kg-day for hexachlorobenzene and was 0.75 mg/kg-day for PCNB.

Table 8-2. Summary of Surveyed Human Health Hazard Data for Pentachlorothiophenol (PCTP)

Organ/System	Study Type	Doses	POD	Health Effect	Reference
Liver	2-year feeding dog study	0, 30, 180, 1080 ppm Pentachloronitrobenzene	RfD: 3E-3 mg/kg-d NOEL: 30 ppm (0.75 mg/kg-d)	Increased liver weight, ALP, and cholestatic hepatosis	U.S. EPA (1987)
Liver	2 year feeding Sprague-Dawley rats	0, 0.32, 1.6, 8.0, 40 ppm Hexachlorobenzene	RfD: 8E-4 mg/kg-d NOEL: 1.6 ppm (0.08 mg/kg-d)	Increased hepatic centrilobular basophilic chromogenesis	U.S. EPA (1988)

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