B2-1.0 PENTACHLOROPHENOL (PCP)

B2-1.1 Background Information

PENTACHLOROPHENOL **Timbertox #10**

IUPAC: pentachlorophenol

CAS: pentachlorophenol

CASRN: 87-86-5

CONTAMINANTS:
Trichlorophenol
Tetrachlorophenol
Hexachlorobenzene (HCB)
Polychlorinated dibenzo-p-dioxins
- (hexachlorodibenzo-p-dioxin (HxCDD))
- (2,3,7,8-tetrachlorobenzo-p-ioxin (TCDD))

Polychlorinated dibenzofurans
Polychlorinated biphenyls (PCBs)

Note: Most of the toxicological studies utilized by the U.S. EPA in concordance with PMRA are older data. Therefore, test materials may contain measurable concentrations of contaminants such as hexachlorodioxins and hexachlorobenzene (U.S. EPA, 2004a).

PCP USAGE

PCP was introduced in the 1903s, and was used in large quantities as a wood preservative. It has also been used as an herbicide, defoliant, bactericide and molluscicide. In recent years its use in agriculture has been restricted in many countries due to its contaminants.

PCP was sprayed at CFB Gagetown on designated plots during the U.S. 1967 Trial only (Table B2-1).

Table B2-1 PCP Usage at CFB Gagetown[a]

Year	Total PCP Applied (kg)	Total Area Treated (ha)
1967	3.3E+01	2.4E+00

[a] Adapted from Demaree and Haws, 1968.

B2-2.0 CHEMICAL AND PHYSICAL PROPERTIES

Formula: C_6HCl_5O

Activity: fungicides (aromatic fungicides); herbicides (unclassified herbicides); insecticides (organochlorine insecticides); molluscicides; plant growth regulators (defoliants)

Notes: This substance is considered by the International Organization for Standardization not to require a common name. The name "**PCP**" is approved by the Japanese

Ministry of Agriculture, Forestry and Fisheries and the Weed Science Society of America. The sodium salt is also considered by the International Organization for Standardization not to require a common name, see sodium pentachlorophenoxide.

Structure:

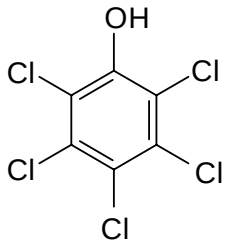


Figure B2-1 PCP CASRN 87-86-5

Table B2-2 Chemical and Physical Properties of PCP

Chemical/Physical Property	Result	Reference
Boiling Point	309-310°C	FAO, 1996; ATSDR, 2001
Colour/Form	Pure: Colourless or white Crystalline solid	Verschueren, 1983
	Crude: dark grey to brown pellets or powder	
Dissociation Constant (pKa)	4.7	JW, 2006
Henry's Law constant	$2.75x10^{-6}$ atm·m^3/mol	ATSDR, 2001
	$3.46x10^{-6}$ atm·m^3/mol	Lyman *et al*., 1982
	$2.45x10^{-8}$ atm·m^3/mol at 25°C	JW, 2006
Log K_{ow}	5.01	Verschueren, 1983
	5.86	JW, 2006
Melting Point	190°C	ATSDR, 2001
	191°C (anhydrous)	FAO, 1996
	174°C (monohydrous)	FAO, 1996
Molecular Weight	266.35 g/mol	ATSDR, 2001; JW, 2006
Odour	Phenolic; very pungent (only when hot)	ATSDR, 2001
Vapour Pressure	2 mPa at 20°C	FAO, 1996
	$1.1x10^{-4}$ mm Hg at 25°C	U.S. EPA, 1979; JW, 2006
Water Solubility	14 mg/L at 20°C and 25°C	ATSDR, 2001; JW, 2006
	20 mg/L at 30°C	FAO, 1996

B2-3.0 PMRA EVALUATION

Currently PMRA has been working very closely with the U.S. EPA on the re-evaluation of PCP (PMRA, 2005). The U.S. EPA consultation process includes the release of preliminary risk assessments for comments by stakeholders and the public, prior to finalizing the risk assessments. Preliminary documents for PCP and its contaminants were released in 2004 and 2005, respectively. The preliminary documents are no longer available for comment; however the final re-registration document (RED) produced by the U.S. EPA and the re-registration decision document produced by PMRA have not yet been released.

B2-4.0 TOXICOLOGICAL SUMMARY

B2-4.1 Human Health Effects

Table B2-3 Human Health Effects Resulting from Acute Exposure to PCP[a,b]

Exposure	Effects	Response
Acute	HEENT	Slight mydriasis; corneal opacity; corneal numbness
	Cardiovascular	Cardiac dilatation; tachycardia; heart failure; tachypnea; hypotension; may sensitize the heart to catecholamines
	Respiratory	Bronchitis; tachnypnea
	Neurologic	Rapidly progressing and profound coma (severe intoxications); seizures; dizziness; headache
	Gastrointestinal	Anorexia; inflamed gastric mucosa; gastrointestinal upset
	Hepatic	Centrilobular necrosis
	Genitournary	Renal tubular degeneration
	Acid-Base	Metabolic acidosis
	Hematologic	Anemia; hemolysis
	Dermatologic	Irritation; dermatitis
	Musculoskeletal	Muscular collapse, death, rapid rigor mortis (severe poisoning); rhabdomyolysis
	Endocrine	Hyperglycemia; glucosuria

HEENT Head, Ears, Eyes, Nose, Throat
[a] Rumack and Hall, 2006
[b] MEDITEXT®, 2006

Chronic PCP poisoning may produce anorexia, weight loss, weakness, dizziness, headaches and anxiety (MEDITEXT®, 2006; Rumack and Hall, 2006).

B2-4.2 Health Effects by Route of Exposure

B2-4.2.1 Oral Exposure

The acute oral toxicity of PCP is high (Toxicity Category II) (U.S. EPA, 2004a).

B2-4.2.1.1 Death

Table B2-4 Mammalian LD_{50} values Resulting from Oral Exposure to Pentachlorophenol

Test Organism (Species/Sex)	Grade	LD_{50} (mg/kg)	Reference
Acute			
Mouse (F)	Pure (~99% a.i.)	117	Borzelleca *et al*., 1985
Mouse (M)	Pure (99% a.i.)	129	Renner *et al*., 1986
Mouse	--	130	Demidenko, 1969
Mouse (F)	Pure (99% a.i.)	134	Renner *et al*., 1986
Mouse (M)	Pure (~99% a.i.)	177	Borzelleca *et al*., 1985
Rat	Technical	27[a,b]	Deichmann *et al*., 1942
Rat	Technical	50	St. Omer and Gadusek, 1987
Rat	Technical	78 [b]	Deichmann *et al*., 1942

Table B2-4 Mammalian LD_{50} values Resulting from Oral Exposure to Pentachlorophenol

Test Organism (Species/Sex)	Grade	LD_{50} (mg/kg)	Reference
Rat	--	184	Demidenko, 1969
Rat	Technical	211[b]	Deichmann *et al*., 1942

[a] 0.5% in fuel oil.
[b] Sodium PCP.

B2-4.2.1.2 Systemic Effects

Female Sherman rats were orally exposed to both technical and purified PCP for eight months. Rats exposed to the technical grade PCP exhibited increased liver to body weight ratios at a dose level of 1 mg/kg (Kimbrough and Linder, 1978). However, a dosage of 30 mg/kg of the purified PCP was required to illicit the same response (Goldstein *et al*., 1977). Therefore, it is believed that the impurities in PCP contribute significantly to the observed liver toxicity.

Table B2-5 Systemic Effects Resulting from Oral Exposure to PCP

Test Type	Test Organism (Species)	Grade	Dose (Duration)	Response	Reference
Chronic					
Chronic	Dog (Beagle)	90.9% a.i.	1.5 mg/kg/day (1 year)	Increased incidence of gross stomach lesions consisting of multiple raised foci (M); dark, discoloured liver (M); increased incidence of lymphocytic mucosal inflammation in the stomach	Mecler, 1996
Chronic	Dog (Beagle)	90.9% a.i.	6.5 mg/kg/day (1 year)	Decreased mean body weight; decreased red cell count, hemoglobin and hemocrit; elevated activity of alkaline phosphatase, alanine aminotransferase and aspartate aminotransferase; increased gamma-glutamyltranspeptidase activity (M); elevated absolute and relative liver and thyroid (F) weight	Mecler, 1996

(M) Effects observed in males only
(F) Effects observed in females only

B2-4.2.1.3 Neurological Effects

Available data for PCP indicate the potential for nervous system effects *in vitro*. Subchronic exposure in the mouse suggested evidence of neurologic effects. Chronic exposures have produced clear evidence of neurological effects. The U.S. EPA (2004a) has required an acute neurotoxicity study for PCP as a condition of reregistration.

Table B2-6 Neuorological Effects Resulting from Oral Exposure to PCP

Test Type	Test Organism (Species)	Grade	Dose (Duration)	Response	Reference
Sub-Chronic					
Sub-chronic	Mice (B6C3F1)	Technical	200-1,800 ppm	Decreased motor activity and rotarod performance; increased motor activity and startle response (F)	U.S. EPA, 2004a

(F) Effects observed in females only.

B2-4.2.1.4 Reproductive/Developmental Effects

No studies that adequately assessed the reproductive toxicity of PCP in humans were found. A possible association between PCP exposure and reproductive effects was found in women exposed to technical-grade PCP from out-gassing wood panels treated with a wood preservative containing PCP (ATSDR, 2001). However, study limitations prevented the study from being used to establish a causal relationship (ATSDR, 2001).

A number of animal studies provide evidence that the reproductive system is a sensitive target of PCP toxicity (ATSDR, 2001). Adverse reproductive effects were observed in animals following oral exposure to technical-grade and pure PCP. In a two-generation reproductive toxicity study in rats, decreased fertility was observed the first generation exposed to 60 mg/kg/day PCP (88.9% a.i.) (Hoberman, 1997). Decreased frequency of second mating, decreased birth rate for the second mating, and increased severity of cystic uterine gland were observed in mink exposed to 1 mg/kg/day (Beard *et al.*, 1997). In contrast, no reproductive effects were observed in a multi-generation study in mink using the same dietary concentration (Beard and Rawlings, 1998). No effect on fertility was observed in sheep exposed to 1 mg/kg/day prior to mating and throughout gestation and lactation (Beard *et al.*, 1999). The mink studies conducted by Beard and Rawlings (1997; 1998) are significant as CalEPA and ATSDR used them to established reference dose levels for both chronic and acute PCP exposures.

Schwetz *et al*. (1974) examined the difference between pure and technical-grade PCP on developmental toxicity (Table B2-6). The pure PCP was slightly more toxic than the technical-grade in terms of maternal body weight gain, fetal resorptions, fetal body weight and occurrence of fetal anomalies. Schwetz *et al*. (1974) stated that the maternal dose resulting in mortality of one half of the embryos was 16 mg/kg/day pure PCP *versus* 44 mg/kg/day for technical grade PCP.

Table B2- 7 Reproductive and Developmental Effects Resulting from Oral Exposure to PCP

Test Organism (Species)	Exposure	Grade	Dose (Duration)	Response	Reference
Rat (Sprague-Dawley)	Gavage	Commercial (88.4% a.i)	30 mg/kg/day (days 6 through 15 of gestation)	Maternal effects: decreased maternal weight gain; increased fetal absorption Fetal effects: decreased fetal body weight	Schwetz *et al.*, 1974
Rat (Sprague-Dawley)	Gavage	Purified (>98% a.i)	30 mg/kg/day (days 6 through 15 of gestation)	Maternal effects: decreased maternal weight gain; increased fetal absorption Fetal effects: decreased fetal body weight; decreased crown rump length	Schwetz *et al.*, 1974
Rat (Sprague Dawley)	Gavage	(88.9% a.i)	30 mg/kg/day (2 generation study)	Maternal effects: decreased body weight gain and body weight; decreased average testicular spermatid count and testis weight	Hoberman, 1997
Rat (Sprague-Dawley)	Gavage	Purified (>98% a.i)	50 mg/kg/day (days 6 through 15 of gestation)	Number of litters was severely limited	Schwetz *et al.*, 1974
Rat (Sprague Dawley)	Gavage	(88.9% a.i)	60 mg/kg/day (2 generation study)	Maternal effects: decreased body weight and body weight gain; decreased gestational and lactational body weights; decreased fertility index and number of litters; increased incidence of sperm with broke flagellum; decreased testicular spermatid count; decreased testis weight; decreased brain weight and increased liver weight; increased incidence of macroscopic and microscopic pathology Fetal effects: increased number of days to vaginal patency (F) and preputial separation (M); reduced mean litter size, number of live pups and viability index; decreased weight of the liver, brain, spleem and thymus	Hoberman, 1997
Rat (Crl:CD BR VAF)	Gavage	--	80 mg/kg/day (days 6 through 15 of gestation)	Maternal effects: increased number of resorptions; decreased litter size Fetal effects: reduced mean fetal weights; increased number of fetuses with external, visceral and/or skeletal malformations/variations	Hoberman, 1994
Rat (Sprague-Dawley)	Diet	Purified	60 ppm (181 d)	Maternal effects: decreased pregnancy rate	Welsh *et al.*, 1987
Rat (Sprague-Dawley)	Diet	Purified	200 ppm (181 d)	Fetal effects: decreased body weight; increased incidence of misshapen centra; increased incidence of total skeletal variations	Welsh *et al.*, 1987

Table B2- 7 Reproductive and Developmental Effects Resulting from Oral Exposure to PCP

Test Organism (Species)	Exposure	Grade	Dose (Duration)	Response	Reference
Rat (Sprague-Dawley)	Diet	Purified	600 ppm (181 d)	Maternal effects: decreased body weight gain; increased total litter resorption	Welsh *et al.*, 1987
				Fetal effects: decreased number of viable fetuses	
Rabbit (New Zealand white)	Gavage	--	15 mg/kg/day (days 6 through 18 of gestation)	Maternal effect: reduced weight gain	Hoberman, 1994
Rabbit (New Zealand white)	Gavage	--	30 mg/kg/day (days 6 through 18 of gestation)	Maternal effect: reduction in mean food consumption	Hoberman, 1994
Mink	Diet	Not Reported	1 mg/kg/day (Multi-generation study)	Decreased serum thyroxine levels; decreased relative thyroid weight (F)	Beard and Rawlings, 1998
Mink	Diet	Not Reported	1 mg/kg/day (1 generation study)	Decreased proportion of mated females accepting a second mating and the proportion of mink that whelped; increased severity of cystic uterine glands prior to mating and during gestation and lactation periods	Beard *et al.*, 1977

(F) Effects observed in females only

B2-4.2.1.5 No Observed Adverse Effect Levels

Table B2-8 NOAELs and LOAELs for Oral Exposure to PCP[a]

Test Organism (Species)	Grade	Effect	Value (mg/kg/day)	Endpoint	Reference
Acute					
Rat (Wistar)(M)	--	NOAEL	10	Increased hepatic glycogen	Nishimura *et al*., 1982
Sub-chronic					
Mice (C5751/6J)	--	LOAEL	5	Tumour growth susceptibility	Kerkvliet *et al*., 1982
Mice (B6C3F1)	Multiple grades	NOAEL	1200-1,800	Neurological toxicity	U.S. EPA, 2004a
Rat (Sprague Dawley)	--	LOAEL	5	Fetal resorptions	Schwetz *et al*., 1974
Rat (Wistar)(M)	--	NOAEL	1.21	Anemia; centrilobular vacuolization in liver	Knudsen *et al*., 1974
Rat (Wistar)(F)	--	NOAEL	1.64	Anemia; centrilobular vacuolization in liver	Knudsen *et al*., 1974
Rat (Sprague Dawley)	--	NOAEL	3	Hepatocellular degeneration and necrosis	Johnson *et al*., 1973
Pig	--	NOAEL	5	Leukopenia	Greichus *et al*., 1979
Chronic					
Rat (Sprague Dawley)	--	NOAEL	3	Embryo-lethality	Schwetz *et al*., 1978
Rat (Sprague Dawley)(F)	--	NOAEL	3	Increased liver enzyme activity; increased liver and kidney pigmentation	Schwetz *et al*., 1978
Rat (Sherman)	--	NOAEL	6	Increased hepatic enzymes and porphyrin	Goldstein *et al*., 1977
Rat (Sprague Dawley)(M)	--	NOAEL	10	Increased liver enzyme activity; increased liver and kidney pigmentation	Schwetz *et al*., 1978
Dog (Beagle)	90.9% a.i.	LOAEL	1.5	Liver effects	Mecler, 1996
Dog (Beagle)	90.9% a.i	NOAEL	6.5	Nervous system anatomy or function	Mecler, 1996

[a] Obtained from CalEPA, 1997; U.S. EPA, 1993; U.S. EPA, 2004.

Table B2-9 Reproductive and Developmental NOAEL and LOAEL Values from Dietary Exposure to PCP[a]

Test Organism (Species)	Effect	Grade	Value (mg/kg/day)	Endpoint	Reference
Rat (Sprague Dawley)	LOAEL	(88.9% a.i.)	30	Developmental toxicity (decreased group mean litter weight)	Hoberman, 1997
Rat (Sprague-Dawley)	LOAEL	Commercial (88.4% a.i.)	30	Developmental toxicity (decreased fetal body weight and crown rump length)	Schwetz *et al.*, 1974
Rat (Sprague Dawley)	LOAEL	(88.9% a.i.)	30	Maternal systemic toxicity (decreased body weight and weight gain; adverse testicular effects)	Hoberman, 1997
Rat (Crl:CD BR VAF)	LOAEL	--	80	Maternal toxicity (reduced body weight gain); Developmental toxicity (increased resorptions; reduced fetal weight; skeletal malformations/variations)	Hoberman, 1994
Rat (Sprague Dawley)	NOAEL	(88.9% a.i.)	10	Maternal systemic toxicity; Reproductive toxicity	Hoberman, 1997
Rat (Sprague-Dawley)	NOAEL	Commercial and Purified[b]	15	Maternal toxicity (body weight effect)	Schwetz *et al.*, 1974
Rat (Sprague-Dawley)	NOAEL	Commercial (88.4% a.i.)	15	Developmental toxicity	Schwetz *et al.*, 1974
Rat (Crl:CD BR VAF)	NOAEL	--	30	Maternal and developmental toxicity	Hoberman, 1994
Rat (Sprague Dawley)	NOAEL	Purified	43	Fertility	Welsch *et al.*, 1987
Rabbit (New Zealand white)	NOAEL	--	15	Maternal toxicity	Hoberman, 1994
Rabbit (New Zealand white)	LOAEL	--	30	Maternal toxicity (minimally reduced body weight gain; reduced food consumption)	Hoberman, 1994
Rabbit (New Zealand white)	NOAEL	--	30	Maternal mortality or toxicity; external, visceral and skeletal fetal malformations; Developmental toxicity	Hoberman, 1994
Mink	NOAEL	Not reported	1	Proportion of mink that accepted the first mating; proportion of mink with visible implantation sites; no alterations in reproductive hormones	Beard *et al.*, 1977
Mink	NOAEL	Not Reported	1	Reproductive effects	Beard and Rawlings, 1998

[a] Obtained from CalEPA, 1997; ATSDR, 2001; CalEPA, 2004; U.S. EPA, 2004a.
[b] Commercial grade (88.4% a.i.); Purified grade (>98% a.i.).

B2-4.2.2 Dermal Exposure

The acute toxicity of PCP is low for dermal toxicity (Toxicity Category IV) and primary dermal irritation (Toxicity Category III) (U.S. EPA, 2004a). No dermal sensitization was observed with the technical test material. (U.S. EPA, 2004a).

B2-4.2.2.1 Death

Table B2-10 Mammalian Acute LD_{50} Value Resulting from Dermal Exposure to PCP

Test Organism (Species/Sex)	LD_{50} (mg/kg)	Reference
Rat	96	CalEPA, 1997
Species not identified	> 3.980	Norris, 1972

B2-4.2.2.2 Systemic Effects

Table B2-11 Systemic Effects Resulting from Dermal Exposure to PCP

Test Organism (Species)	Dose (mg/kg/day) (Duration)	Response	Reference
Sub-Chronic			
Rat (Sprague-Dawley)	≥100 (90 d)	Erythema (grade 1-2); decreased platelet counts (F)	Osheroff *et a*l., 1994
Rat (Sprague-Dawley)	≥500 (90 d)	Increased total white blood cell counts and absolute lymphocyte counts (F); increased alanine and aspartate aminotransferase activities; increased cholesterol (F); increased kidney weight (F); increased incidence of hepatocellular degeneration and chronic inflammation	Osheroff *et a*l., 1994
Rat (Sprague-Dawley)	1,000 (90 d)	Increased absolute liver weight; increased kidney weight (M)	Osheroff *et a*l., 1994

B2-4.2.2.3 Neurological Effects

There was no evidence of neurological effects through dermal exposure. During a 90 day dermal toxicity study in Sprague-Dawley rats, there were no signs of treatment-related effects at the highest dosage (1,000 mg/kg/day) on nervous system anatomy or function (Osheroff *et al*., 1994). There were no clinical signs of neurotoxicity and no reported abnormalities of the brain, spinal cord, or pituitary.

B2-4.2.2.4 Reproductive/Developmental Effects

No data found.

B2-4.2.2.5 No Observed Adverse Effect Level

Table B2-11 NOAELs and LOAELs for Dermal Exposure to PCP[a]

Test Organism (Species)	Effect	Value (mg/kg/day)	Endpoint	Reference
Sub-Chronic				
Rat (Sprague-Dawley)	LOAEL	500	Systemic toxicity (enzyme induction; minimal to mild hepatocellular degeneration; chronic inflammation)	Osheroff *et al*., 1994
Rat (Sprague-Dawley)	NOAEL	100	Systemic toxicity	Osheroff *et al*., 1994
Rat (Sprague-Dawley)(F)	NOAEL	1,000	Group mean body weight or weight gain; mortality; clinical signs of toxicity	Osheroff *et al*., 1994

[a] Obtained from U.S. EPA, 2004a.

B2-4.2.3 Inhalation Exposure

B2-4.2.3.1 Death

Table B2-12 Mammalian acute LD_{50} Value Resulting from Inhalation Exposure to PCP

Test Organism (Species/Sex)	LD_{50}	Reference
Rabbit	201 mg/kg	FAO, 1996
Mice	225 mg/m^3	CalEPA, 1997
Rat	335 mg/m^3	CalEPA, 1997

B2-4.2.3.2 Systemic Effects

No data found.

B2-4.2.3.3 Neurological Effects

There is limited data on the neurotoxicity of inhaled PCP in humans (ATSDR, 2001). However, in a worker exposed to PCP dust, signs of central nervous system toxicity and cerebral edema with focal swelling of the myelin sheath were observed (Gray *et al*., 1985).

B2-4.2.3.4 Reproductive/Developmental Effects

No data found.

B2-4.2.3.5 No Observed Adverse Effect Level

No data found.

B2-4.3 Carcinogenicity

The U.S. EPA (1993) classified PCP as a probable human carcinogen (2B). This classification was based on inadequate human data and sufficient evidence of carcinogenicity in animals. Statistically significant increases in the incidence of multiple biologically significant tumour types were observed in one or both sex of mice using two different preparations of technical grade PCP (U.S. EPA, 1993).

IARC (1991) classified PCP as possibly carcinogenic to humans (Group 2B) based on inadequate evidence in humans and sufficient evidence in animals to suggest carcinogenicity.

Table B2-13 Animal Carcinogenicity Data[a]

Test Subjects	Exposure	Grade	Dose (mg/kg/day)	Response	Reference
Mice (Sutter)	Dermal	20% Commercial Grade PCP in benzene	Twice weekly (13 weeks)	No significant increase in tumour incidence	Boutwell and Bosch, 1959
Mice	Gavage	EC-7	17 (18 months)	No significant increased incidence of tumours	Innes *et al*., 1969
Mice (B6C3F1)	Diet	Technical Grade	35 (2 years)	Increased incidence of heptacellular adenomas and/or carcinomas as well as benign and malignant pheochromocytomas of the adrenal medulla (M); increased incidence of hemangiosarcoma tumors (F)	NTP, 1989
Mice (B6C3F1)(M)	Diet	90% pure (EC-7)	114-118 (2 years)	Increased incidence of hepatocellular adenomas and/or carcinomas as well as benign and malignant pheochromocytomas of the adrenal medulla (M); Increased incidence of liver tumours and benign and malignant pheochromocytomas (F); vascular tumours observed (F)	NTP, 1989
Rat (Sprague-Dawley)	Diet	90% Pure (Dowicide EC-7 PeCP)	30	No significant increase in tumour incidence	Schwetz *et al*., 1978

[a] Obtained from U.S. EPA, 1993.

In studies with cultured CHO cells, technical grade PCP produced an increase in chromosomal aberrations in the presence, but not the absence of S9 hepatic homogenate activation. Conversely, SCEs were induced only in the absence of S9 hepatic homogenate (NTP, 1989).

One human carcinogencitiy study (Gilbert *et al*., 1990) was available; however, it was classified as inadequate by the U.S. EPA (1993) due to over a 30% loss of the original cohort for follow-up.

Cancer Slope Factors

The U.S. EPA (1993) derived an oral slope factor of $1.2x10^{-1}$ $(mg/kg/day)^{-1}$ based upon a feeding study conducted by NTP (1989).

A slope factor of $1.8x10^{-2}$ $(mg/kg/day)^{-1}$ was calculated by CalEPA (2005) and the U.S. EPA (2000) from a cancer potency factor derived by CDHS (1991) from male mouse liver tumour data from an NTP study (1989) using a linearized multistage procedure.

A human equivalent oral cancer slope factor of $8.11x10^{-2}$ $(mg/kg/day)^{-1}$ was also established by the CalEPA (1997) based on carcinogenic effects (adenoma and carcinoma) in male mice in a bioassay (NTP, 1989) .

An oral slope factor of 7.0×10^{-2} $(mg/kg/day)^{-1}$ was calculated by the U.S. EPA (2004c) based on the combined incidence of hemangiosarcomas, liver adenomas/carcinomas, and adrenal pheochromocytomas observed in female mice from a study conducted by the National Toxicology Program (NTP, 1989). The slope factor was calculated as the geometric mean of the individual slope factors derived from two data sets: female mouse data for technical grade and Dowicide EC-7 PCP (U.S. EPA, 2004c).

A slope factor of $1.2x10^{-1}$ $(mg/kg/day)^{-1}$ was selected for the risk assessment purposes of this report.

Populations at Special Risk

There is some evidence that young children are more susceptible than older children and adults to the toxic effects of PCP, associated with the uncoupling of oxidative phosphorylation (ATSDR, 2001). Chapman and Robson (1965) observed signs of hyperthermia in a 3 year old child exposed to PCP in contaminated bath water; however, no signs were observed in the older children or adults. In addition, pre-weaning and adult rats have been reported to have lower oral LD_{50}s for technical-grade PCP than juvenile rats (St. Omer and Gadusek, 1987). Therefore, it is possible that differences in age-specific sensitivity may also occur in humans (ATSDR, 2001). These adverse effects, however, may be a direct result of PCP contaminants as a crude formulation was utilized.

In developmental toxicity studies in rats and rabbits there has been no indication of increased sensitivity of young animals to pre- and/or post-natal exposure to PCP (U.S. EPA, 2004a). However, contaminants of PCP formulations are teratogenic agents. Therefore, the U.S. EPA (2004a) determined that PCP may produce defects in the offspring of laboratory animals, and that exposure to PCP during pregnancy should be avoided.

Populations at a greater-than average risk of suffering toxic effects from exposure to PCP include people laboring in hot environments, those with an inability or decreased ability to disperse body heat, geriatric and pediatric subpopulations, and those that are malnourished or consume an unbalanced diet (ATSDR, 2001). In addition, those with impaired liver or kidney function may be unusually susceptible to the effects of PCP (ATSDR, 2001).

B2-4.4 Toxicokinetics

B2-4.4.1 Absorption

PCP has been shown to be readily absorbed by oral, inhalation and dermal exposure routes (U.S. EPA, 2004a; FAO, 1996). Absorption from the dermal exposure has been shown to range from 24% in rhesus monkeys (Wester *et al*., 1993) to 40% in rats (Selim, 1985). Human volunteers have been shown to absorb 76 to 88% of the total potential dose through PCP exposure through inhalation (Casarett *et al*., 1969). In addition, rats absorbed 70 to 75% of a PCP dose from a single 20 minute inhalation exposure (Hoben *et al*., 1976).

Dermal Absorption

The U.S. EPA (2004a) used a dermal absorption factor of 40%. This value is based on a dermal absorption study in which radiolabeled PCP was applied to the skin of young Sprague-Dawley rats. At 8 and 24 hours post-application the calculated absorption was 40 and 60%, respectively (Selim, 1985).

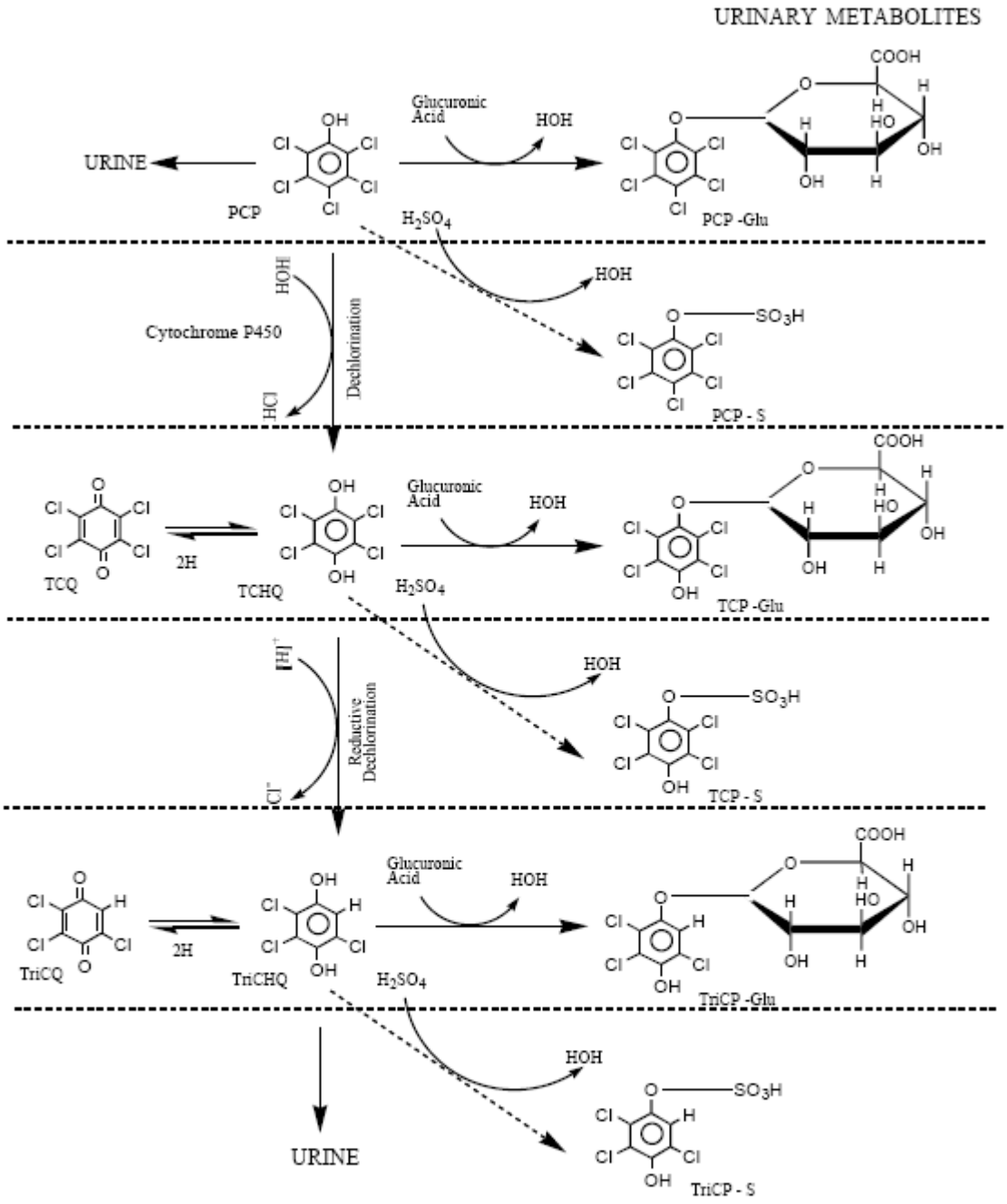
B2-4.4.2 Distribution

Absorbed PCP is distributed to the liver, lungs, kidneys, blood, fat tissues and brain (ATSDR, 2001). The binding of PCP to plasma proteins plays a significant role in the distribution of PCP within the body (Braun *et al*., 1977; Gómez-Catalán *et al*., 1991). The levels in the liver and kidney are particularly high, whereas those in the fat, brain and muscle are relatively low (Larsen *et al*., 1972; Braun *et al*., 1977).

B2-4.4.3 Metabolism

Combined human and animal data indicate that PCP is metabolized in the liver. The major pathways are oxidative dechlorination to form tetrachlorohydroquinone (TCHQ) and conjugation to form the glucuronide (ATSDR, 2001).

PCP is metabolized in rats to tetrahydroquinone *via* 2,3,5,6-tetrachlorophenol as a main degradative pathway. PCP is also biotransformed to trichlorohydroquinone *via* 2,3,4,6-tetrachlorophenol and 2,3,4,5-tetrachlorophenol through a minor pathway (U.S. EPA, 2004a). PCP, trichlorophenol and tetrachlorophenol can be conjugated with glucuronic acid or sulfate (U.S. EPA, 2004a). For instance, gulcuronides of PCP were the major urinary metabolite observed after oral doses of PCP (Ahlborg, 1978; Braun, 1977).



PCP = pentachlorohenol; PCP-Glu = pentachlorophenol-β-glucuronide; PCP-S = pentachlorophenylsulfate;
TCHQ = tetrachloro-p-hydroquinone; TCP-Glu = tetrachlorophenol-β-glucuronide; TCP-S = tetrachlorophenylsulfate;
TCQ = tetrachloroquinone; Tri CHQ = trichloro-p-hydroquinone; Tri CP-Glu = trichlorophenyl-β-glucuronide;
Tri CP-S = trichlorophenylsulfate; Tri CQ = trichloro-p-quinone

Figure B2-2 Proposed metabolic scheme for PCP (ATSDR, 2001)

B2-4.4.4 Elimination and Excretion

PCP and its metabolites are excreted mainly in the urine by all routes of exposure (ATSDR, 2001; U.S. EPA, 2004a). Approximately 12 to 74% of PCP ingested by humans was eliminated as PCP and its glucoronide conjugate, respectively (Braun *et al*., 1979). In addition, Reigner *et al*. (1991) observed a 60% recovery in urine after PCP exposure through ingestion and injection. Fecal elimination of PCP accounted for 4% of the total oral dose in humans, 4 to 34% of the oral dose in rodents, and 4 to 17% in monkeys (ATSDR, 2001). Trace amounts were eliminated in expired air.

Table B2-14 Kinetics of PCP Elimination from Test Organisms[a]

Test Organism/Compound	Location	Half-life	Reference
Rat	--	2-11 hours	Reigner *et al*, 1991 ; Braun *et al*., 1977
Mice	--	5-6 hours	Reigner *et al*., 1992
PCP glucuronide elimination	Urine	13 hours	CalEPA, 1997
PCP elimination	Urine	33 hours	CalEPA, 1997
Humans	plasma	30.2 ± 4.0 hours	U.S. EPA, 2004a
Monkey	--	72-84 hours	Bruan and Sauerhoff, 1976

[a] Obtained from CalEPA, 1997; ATSDR, 2001; U.S. EPA, 2004a.

B2-4.5 Exposure Limits

Exposure limits are estimates of a daily oral exposure to the human population (including sensitive subgroups) that is not likely to cause deleterious effects during a lifetime. Exposure limits can be derived from a NOAEL, LOAEL, or benchmark dose, with uncertainty factors applied to reflect the limitations of the data used.

Jurisdictional bodies derive varying exposure limits. For instance, the U.S. EPA and CalEPA determine a reference dose (RfD); whereas ATSDR establishes minimal risk levels (MRLs). Health Canada, PMRA and WHO express exposure limits as acceptable daily intakes (ADIs).

Table B2-15 Existing Oral RfD Values for PCP Exposures[a]

Daily Reference Dose (mg/kg)	Reference	Endpoint	Study	Reference	Grade	NOEL (mg/kg/day)	Uncertainty Factor	Study Classification
Acute/Short-term (1-7 days)								
0.005[b]	ATSDR, 2001	Increased occurrence of delayed ossification of the skull	Developmental Rat study	Schwetz *et al.*, 1974	--	5 (LOEL)	1,000	--
0.3	U.S. EPA, 2004a	Increased resorptions; reduced fetal weight; skeletal malformations	Developmental Rabbit toxicity study	Hoberman, 1994	--	30	100	--
Intermediate-term (7 days- Several months)								
0.001[b]	ATSDR, 2001	Increased severity of cystic uterine glands; decreased proportions of mink accepting a second mate; number of mink whelping	Reproductive Mink toxicity	Beard *et al.*, 1997	Not Reported	1 (LOEL)	1,000	--
Long-term (6 months to lifetime)								
0.0003[c]	CalEPA, 2004	a) Decreased serum thyroxine concentrations and relative thyroid weight b) Thyroid/neurodevelopment	a) Multigenerational oral mink study b) Developmental lamb toxicity study	Beard and Rawlings, 1998; 1999	Analytical	1 (LOEL)	3,000	--
0.001[b]	ATSDR, 2001	Decreased serum thyroxine concentrations and relative thyroid weight	Multigenerational oral mink study	Beard and Rawlings, 1998	Not Reported	1 (LOEL)	1,000	--
0.03	U.S. EPA, 1993; CalEPA, 1997	Liver and kidney pathology	Rat oral chronic study	Schwetz *et al.*, 1978	--	3	100	High confidence in study; Medium confidence in RfD

[a] Obtained from U.S. EPA, 1993; ATSDR, 2001; CalEPA, 2004a.

[b] Minimal Risk Level (MRL)- estimate of daily human exposure to a hazardous substance at or below which that substance is unlikely to pose a measurable risk of harmful (adverse), noncancerous effects. MRLs are calculated for a route of exposure (inhalation or oral) over a specified time period (acute, intermediate, or chronic). MRLs should not be used as predictors of harmful (adverse) health effects.

[c] Child Specific Reference Dose (chRD).

The U.S. EPA (1993) established a chronic RfD of 0.03 mg/kg/day based upon a NOAEL of 3 mg/kg/day for a chronic rat study (Schewtz *et al*., 1978) and an uncertainty factor of 100. Pigmentation of the liver and kidneys was observed in females at a dose levels greater than 10 mg/kg/day and at 30 mg/kg/day in males. At the time of publication the study conducted by Schwetz *et al*. (1978) was the only chronic study with oral exposure within the available literature. Both ATSDR (2001) and CalEPA (2004) based their chronic MRL and chRD values of 0.001 and 0.0003 mg/kg/day, respectively, on a LOAEL of 1 mg/kg/day for decreased serum thyroxine concentrations and decreased relative thyroid weight during a multigenerational mink study conducted by Beard and Rawlings (1998; 1999). ATSDR (2001) applied a safety factor of 1,000 to account for the use of a LOAEL, interspecies extrapolation and human variability. CalEPA (2004) applied a safety factor of 3,000 with an additional factor of 3 for database deficiency for developmental neurotoxicity.

The U.S. EPA (2004a) developed an acute oral RfD of 0.3 mg/kg/day based upon a NOEL of 30 mg/kg/day for increased resorptions, reduced fetal weight and skeletal malformations for a developmental toxicity study in rabbits (Hoberman, 1994). The Health Effects Division Hazard Identification Advisory Committee determined that the ten fold safety factor for enhanced sensitivity of infants and children should be removed, therefore, only an uncertainty factor of 100 was applied. ATSDR (2001) selected an acute MRL of 0.005 mg/kg/day based upon a LOAEL of 5 mg/kg/day for developmental effects during a developmental study for rats (Schewetz *et al*., 1974) and a safety factor of 1,000 (10 for LOAEL, 10 for interspecies extrapolation, and 10 for human variability).

Table B2-16 Summary of the Toxicological Dose and Endpoints for the PCP used in Human Risk Assessment by the U.S. EPA (2004a)

Exposure Scenario	Reference Dose (mg/kg/day)	Endpoint	Study	NOEL (mg/kg/day)	LOEL (mg/kg/day)	MOE	Reference
Dermal[a] Short-term (1-7 days)	0.3	Increased resorptions; reduced fetal weight; skeletal malformations	Developmental Rabbit toxicity study	30	80	100	Hoberman, 1994
Dermal Intermediate-term (7 d to several months)	0.3	Increased resorptions; reduced fetal weight; skeletal malformations	Developmental Rabbit toxicity study	30	80	100	Hoberman, 1994

Table B2-16 Summary of the Toxicological Dose and Endpoints for the PCP used in Human Risk Assessment by the U.S. EPA (2004a)

Exposure Scenario	Reference Dose (mg/kg/day)	Endpoint	Study	NOEL (mg/kg/day)	LOEL (mg/kg/day)	MOE	Reference
Dermal Long-term (several months to life time)	0.005	Increased liver weight and alkaline phosphatase activity; increased incidence of granular cytoplasmic pigment accumulation in the liver	Chronic toxicity in dogs	--	1.5	300	Mecler, 1996

MOE Margin of exposure- The LED_{10} or other point of departure divided by the actual or projected environmental exposure of interest.

[a] Since an oral NOEL was selected, a dermal absorption rate of 40% should be used for correcting he oral dose to a dermal dose for risk assessments.

Inhalation Exposure

The CalEPA (1997) has calculated a chronic inhalation reference exposure level of 0.1 mg/m^3 based on a route to route extrapolation of EPA's chronic RfD. No other data are currently available to support an inhalation exposure limit for PCP.

Based on the available general population (B2-15) and occupational reference doses (Table B2-16), and available slope factors (Section B2-4.3), the following exposure limits were selected for the risk assessment purposes of this report (Table B2-17).

Table B2-17 Summary of Selected TRVs for Pentachlorophenol

COC	TRV Type	Route	TRV value (mg/kg/day)	Major Health Effects	Route of Exposure in Primary Study	Reference
Pentachlorophenol	Slope Factor	Oral	$1.2x10^{-1}$[a]	Carcinogenic effects (adenoma and carcinoma) in male mice	Oral	U.S. EPA, 1993
	Acute/Short-term RfD (1-7 days)	Oral	0.3	Increased resorptions; reduced fetal weight; skeletal malformations	Oral	U.S. EPA, 2004a
		Dermal				
		Inhalation	NA			
	Intermediate-term RfD (1 weekk to several months)	Oral	0.001[b]	Increased severity of cystic uterine glands; decreased proportions of mink accepting a second mate; number of mink whelping	Oral	ATSDR, 2001
		Dermal	0.3	Increased resorptions; reduced fetal weight; skeletal malformations	Oral	U.S. EPA, 2004a
		Inhalation	NA			
	Long-term RfD (>6 months to lifetime)	Oral	0.03	Liver and kidney pathology	Oral	U.S. EPA, 1993
		Dermal	0.005	Increased liver weight and alkaline phosphatase activity; increased incidence of granular cytoplasmic pigment accumulation in the liver	Oral	U.S. EPA, 2004a
		Inhalation	NA			

[a] Slope factor units: $(mg/kg/day)^{-1}$.
[b] Minimal Risk Level (MRL).

B2-5.0 ENVIRONMENTAL FATE AND EXPOSURE

Current guideline studies requested by the U.S. EPA did not address the environmental fate of micro-contaminants found in PCP (U.S. EPA, 2004b). Please refer to the toxicological profiles on the individual contaminants.

In general the environmental fate and mobility of PCP is dependent on the pH of both soil and water systems. The chemical behaviour and the physical properties of PCP will depend on whether it exists as the phenolate anion (under basic conditions) or the phenol (under acidic conditions)(U.S. EPA, 2004b).

B2-5.1 Air

B2-5.1.1 Transport and Partitioning

PCP is a relatively volatile compound; however, its sodium salt is non-volatile. PCP associated with particulate matter or moisture in the atmosphere will be lost from the atmosphere through wet deposition (U.S. EPA, 2004b).

B2-5.1.2 Transformation and Degradation

In the atmosphere PCP may undergo photolytic degradation through reactions with photochemically produced hydroxyl radicals (U.S. EPA, 2004b).

B2-5.2 Water

B2-5.2.1 Transport and Partitioning

The mobility of PCP in aqueous environments is pH dependant. PCP is a weakly acidic compound (pKa=4.74) in aqueous solutions, and will exist in its ionized form in increasing proportions as the pH increases (U.S. EPA, 2004b). At a pH of 6.5 or greater, PCP will be present as the phenolate anion which is more soluble than the unionized PCP. Therefore, aqueous solubility of PCP increases with increasing pH. The risk of groundwater potential is much greater when the pH of the soil/water solution is more alkaline. Furthermore, PCP will be less soluble in organic matter in soils having a higher pH. However, in general, PCP exists mainly bound to sediments and suspended particles in water (JW, 2005).

B2-5.2.2 Transformation and Degradation

PCP is stable in sterile aqueous medium with a pH ranging between 5 and 9 (U.S. EPA, 2004b). PCP will photolytically degrade in sterile water (pH 5 to 7) (Connor, 1993). Dichloromaleic anhydride was the major photodegradate of PCP at all pHs while tetrachlororescorcinol was the major degradate at pH 5, and a minor degradate at a pH of 9. Other minor degradates at a pH of 5 and 7 were tetrachlorohydroquinone and tetrachlorocatechol (Connor, 1993). These minor degradates may undergo further dechlorination and/or ring cleavages to eventually form chloranil, hydroxyquinones and the major degradate 2,3-dichloromaleic acid (DCM) (U.S. EPA, 2004b).

Chemical degradation of PCP in water occurs mainly through photodegradation (U.S. EPA, 2004b. When exposed to direct sunlight PCP in surface water will rapidly degrade; however, at an increased pH (when the compound is dissociated) photodegradation will occur at an even higher rate (U.S. EPA, 2004b). The major degradates include tetrachlorophenols and trichlorophenols.

Microbial metabolism is the major degradation route for PCP in aerobic and anaerobic aquatic conditions. However, PCP is moderately persistent under both aerobic and anaerobic conditions.

Table B2-18 Half-life of PCP in Water

Conditions	Half-life	Reference
Sterile water (pH 5-7)	13-20 minute	Connor, 1993
Flooded sandy loam soil (Aerobic)	14 days	Schmidt, 1992a
Sterile aqueous medium (pH 5-9)	> 30 days	U.S. EPA, 2004b
Flooded sandy loam soil (Anaerobic)	30-60 days	Schmidt, 1992b

B2-5.3 Sediment and Soil

B2-5.3.1 Transport and Partitioning

Soil adsorption coefficients (K_{oc}) of 1,250 and 1,800 have been reported for PCP (JW, 2006). PCP is moderately mobile in sandy loam soils with low organic carbon (Kd=5.7), and slightly mobile in sandy loam or silt loam soils with high organic carbon (Kd=2.0) (U.S. EPA, 2004). PCP was immobile in a clay loam soil (Weeden, 1993). Groundwater contamination may occur when the soil texture is a sandy loam type.

PCP soil adsorption is highly dependant on the pH of the system. For instance, maximum soil adsorption occurs in soil with pH values of 4.6 to 5.1, whereas no adsorption has been recorded above a pH of 6.8. Studies have also demonstrated that PCP soil desorption rates are also higher at high pH levels (U.S. EPA, 2004b).

B2-5.3.2 Transformation and Degradation

PCP is moderately persistent in the soil. Hydrolysis and photodegradation are not significant routes of PCP degradation in soil under normal soil conditions, especially where microbial degradation and soil adsorption are the dominant degradation processes (U.S. EPA, 2004b).

Microbial metabolism is the major degradation route for PCP in aerobic and anaerobic soil and sediment. At low pH values, however, absorption is a major fate process for PCP in soils (U.S. EPA, 2004b). The major degradation products of PCP are 2,3,6- and 2,4,6-trichlorophenol (U.S. EPA, 2004b). Other minor degradates include pentachloroanisole, 2,3,4,6- and 2,3,5,6-tetrachlorophenol, and 2,3,5- and 2,3,4-trichloropehnol.

Table B2-19 Half-life of PCP in Soil

Conditions	Half-life	Reference
Microbial biodegradation	< 30 days	U.S. EPA, 2004b
Aerobic	< 30 days	U.S. EPA, 2004b
Field conditions	45 days	JW, 2005
Sandy loam soil	63 days	Schmidt, 1992c
Aerobic	> 63 days	U.S. EPA, 2004b

B2-5.4 Other Environmental Media

B2-5.4.1 Transport and Partitioning

PCP has a biconcentration factor ranging between 50 and 5,370, and therefore is expected to bioaccumulate in aquatic environments (JW, 2006). However, because the aqueous solubility of PCP is pH dependant its bioaccumulation potential will also depend on the pH of the aquatic environment (U.S. EPA, 2004b). Studies indicate that bioaccumulation of PCP in fish is greater in acidified lakes than non-acidified lakes in the same geographical regions (Larsson *et al*., 1993). Therefore, bioaccumulation is expected to occur in fish; however, residues are rapidly depurinated (Dionne, 1993). No biomagnification of PCP in the food chain has been reported (U.S. EPA, 2004b).

B2-5.4.2 Transformation and Degradation

Refer to section B2-4.5 Toxicokinetics.

B2-6.0 SUMMARY

Pentachlorophenol (PCP) was introduced in the 1930s, and was used as an herbicide, defoliant, bactericide and molluscicide (U.S. EPA, 2004). While PCP was sprayed at CFB Gagetown on designated plots during the U.S. 1967 Trials (Demaree and Haws, 1968), its use in agriculture has been restricted in many countries due to contaminants of production (hexachlorobenzene, polychlorinated dibenzo-p-dioxins, polychlorinated dibenzofurans, and polychlorinated biphenyls) (U.S. EPA, 2004). Approximately 33 kg of PCP was applied on an area of 2.4 ha at CFB Gagetown.

The acute oral toxicity of PCP is high (Toxicity Category II) (U.S. EPA, 2004). Chronic PCP poisoning in humans may produce anorexia, weight loss, weakness, dizziness, headaches and anxiety (MEDITEXT®, 2006; Rumack and Hall, 2006). Furthermore, the impurities in PCP may also contribute to the development of liver toxicity in humans (U.S. EPA, 2004). PCP has relatively low acute toxicity through the dermal route of exposure (Toxicity Category IV) and is not considered to be a strong primary dermal irritant (Toxicity Category III) (U.S. EPA, 2004). The U.S. EPA (1993) classified PCP as a probable human carcinogen (2B) (U.S. EPA, 1993). This classification was based on inadequate human data and sufficient evidence of carcinogenicity in animals. IARC (1991) classified PCP as a possible human carcinogen (Group 2B) based on inadequate evidence in humans and sufficient evidence in animals.

B2-7.0 REFERENCES

Ahlborg, 1978. Arch. Toxicol. 40: 45-53. Cited In: U.S. EPA, 2004a.

ATSDR. 2001. Toxicological Profile for PCP. Agency for Toxic Substances and Disease Registry, Public Health Service, U.S. Department of Health and Human Services, Atlanta, GA.

Beard, A.P., McRae, A.C., and Rawlings, N.C. 1997. Reproductive efficiency in mink (mustela vison) treated with the pesticides lindane, carbofuran and pentachlorophenol. J Reprod Fertil 111: 21-28. Cited In: ATSDR, 2001.

Beard, A.P., and Rawlings, N.C. 1998. Reproductive effects in mink (mustela vison) exposed to the pesticides lindane, carbofuran and pentachlorophenol in a multigeneration study. J Reprod Fertil 113: 95-104. Cited In: ATSDR, 2001 and CalEPA, 2004.

Beard, A.P., and Rawlings, N.C. 1999. Thyroid function and effects of reproduction in ewes exposed to the organochlorine pesticides lindane or pentachlorophenol (PCP) from conception. J Toxicol Environ Health 58:509-530. Cited In: CalEPA, 2004.

Beard, A.P., Bartlewski, P.M., and Rawlings, N.C. 1999. Endocrine and reproductive function in ewes exposed to the organochlorine pesticides lindane or pentachlorophenol. J Toxicol Environ Health 56:23-46. Cited In: ATSDR, 2001.

Borzelleca, J.F., Hayes, J.R., Condi, L.W., *et al*. 1985. Acute toxicity of monochlorophenols, dichlorophenols and pentachlorophenol in the mouse. Toxicol Lett 29:39-42. Cited In: ATSDR, 2001.

Boutwell, R.K., and D.K. Bosch. 1959. The tumor-promoting action of phenol and related compounds for mouse skin. Cancer Res. 19: 413-424. Cited In: U.S. EPA, 1993.

Braun, W., and Sauerhoff, M. 1976. The pharmacokinetic profile of pentachlorophenol in monkeys. Toxicol. Appl. Pharmacol. 38: 525-533. Cited In: U.S. EPA, 2004a.

Braun, W., Young, J., Blau, G., and Gehring, P. 1977. The pharmacokinetics and metabolism of pentachlorophenol in rats. Toxicol. Appl. Pharmacol. 41: 395-406. Cited In: U.S. EPA, 2004a, ATSDR, 2001 and CalEPA, 1997.

Braun, W.H., Blau, G.E., and Chenoweth, M.B. 1979. The metabolism/pharmacokinetics of pentachlorophenol in man, and a comparison with the rat and monkey. In: Deichmann, W.E. (Ed.). Toxicology and occupational medicine. Elsevier, New York, NY, 289-296. Cited In: ATSDR, 2001.

CalEPA. 1997. Public Health Goal for Pentachlorophenol in Drinking Water. California Environmental Protection Agency, Office of Environmental Health Hazard, Pesticide and Environmental Toxicology Section.

CalEPA. 2004. Development of Health Criteria for School Site Risk Assessment Pursuant to Health and Safety Code Section 901(g): Proposed Child Specific Reference Dose (chRD) for School Site Risk Assessment: Manganese and Pentachlorophenol. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, Integrated Risk Assessment Section.

CalEPA. 2005. Air Toxics Hot Spots Program Risk Assessment Guidelines Part II Technical Support Document for Describing Available Cancer Potency Factors. California Environmental Protection Agency, Office of Environmental Health Hazard Assessment, Air Toxicology and Epidemiology Section.

Casarett, L.J., Benevue, W.L., and Yauger, W.L., *et al*. 1969. Observations on pentachlorophenol in human blood and urine. Am Ind Hyg Assoc J 30:360-366. Cited In: ATSDR, 2001.

CDHS. 1991. Standards for Assessing Health Risks Associated with Exposure to Pentachlorophenol. California Department of Health Services, Toxic Substances Control Program and Administrative Support Division, Technical Services Branch Toxicology and Risk Assessment Section. Berkeley, CA.

Chapman, J.B., and Robson, P. 1965. Pentachlorophenol poisoning from bath water. Lancet 1:1266-1267. Cited In: ATSDR, 2001.

Connor, S. 1993. Pentachlorophenol-Determination of Aqueous Photolysis Rate Constant and Half-Life: Final Report: Lab Project Number: 12836.0692.6112.720: 93-1-4568. Unpublished study prepared by Springborn Labs, Inc. 68 p. Cited In: U.S. EPA, 2004b.

Deichmann, W., Machle, W., Kitzmiller, K.V., *et al*. 1942. Acute and chronic effects of pentachlorophenol and sodium pentachlorophenate upon experimental animals. J Pharmacol Exp Ther 76: 104-117. Cited In: ATSDR, 2001.

Demaree, K.D., and Haws, A.R. 1968. Chemical defoliation of northern tree species. Technical Memorandum 145. Plant Sciences Laboratory, Plant Physiology Division, Department of the Army, Fort Detrick, Frederick, MD.

Demidenko, N.M. 1969. Materials for substantiation of maximally permissible concentration of pentachlorophenol in the atmosphere. Gig. Trud. i Prof. Zabol. 13: 58-60. Cited In: CalEPA, 1997.

Dionne, E. 1993. Pentachlorophenol: Bioconcentration and Elimination of (carbon 14)-residues by Bluegill Sunfish: Lab Project Number: 92-12-4532: 12836.0692.6114.140. Unpublished study prepared by Springborn Laboratories, Inc. 90 p. Cited In: U.S. EPA, 2004b.

FAO. 1996. Decision Guidance Documents: Pentachlorophenol and its salts and esters. Joint Food and Agricultural Organziation/United Nations Environment Program for the Operation of Prior Informed Consent, Geneva.

Gilbert, F., Minn, C., Duncan, R., and Wilkinson, J. 1990. Effects of pentachlorophenol and other chemical preservatives on the health of wood- treating workers in Hawaii. Arch. Environ. Contam. Toxicol. 19(4): 603-609. Cited In: U.S. EPA, 1993.

Goldstein, J., Friesen, M., Linder, R., Hickman, P., Hass, J., and Bergman, H. 1977. Effects of pentachlorophenol on hepatic drug-metabolizing enzymes and porphyrin related to contamination with chlorinated dibenzo-p-dioxins and dibenzofurans, Biochem. Pharmacol. 26: 1549-1557. Cited In: CalEPA, 1997.

Gómez-Catalán, J., To-Figueras, J., Rodamilans, M., *et al*. 1991. Transport of organochlorine residues in the rat and human blood. Arch Environ Contam Toxicol 20: 61-66. Cited In: ATSDR, 2001.

Gray, R.E., Gilliland, R.D., Smith, E.E., *et al*. 1985. Pentachlorophenol intoxication: Report of a fatal case, with comments on the clinical course and pathologic anatomy. Arch Environ Health 40:161-164. Cited In: ATSDR, 2001.

Greichus, Y., Libal, G., and Johnson, D. 1979. Diagnosis and physiologic effects of pentachlorophenols on young pigs. Bull. Environ. Contam. Toxicol. 23: 418-422. Cited In: CalEPA, 1997.

Hoben, H.J., Ching, S.A., and Casarett, L.J. 1976. A study of inhalation of pentachlorophenol by rats: Part IV. Distribution and excretion of inhaled pentachlorophenol. Bull Environ Contam Toxicol 15:466-474. Cited In: ATSDR, 2001.

Hoberman, A.M. 1994. Developmental Toxicity (Embryo-Fetal Toxicity and Teratogenic Potential) Study of Pentachlorophenol Administered Orally *Via* Stomach Tube to New Zealand White Rabbits. Study conducted by Argus Research Laboratories for the Pentachlorophenol Task Force. Cited In: U.S. EPA, 2004a.

Hoberman, A.M. 1997. Oral (Gavage) Two-Generation (One Litter Per Generation) Reproduction Study of Pentachlorophenol in Rats. Study performed by Argus Research Laboratories for the Pentachlorophenol Task Force. Cited In: U.S. EPA, 2004a

HSDB (Hazardous Substances Data Bank). 2005. Pentachlorophenol. U.S. National Library of Medicine's Toxicology Data Network (TOXNET). Available at: http://toxnet.nlm.nih.gov/cgi-bin/sis/htmlgen?HSDB. [September 6, 2006].

IARC. 1991. IARC Summaries and Evaluations: Pentachlorophenol. International Agency for Research on Cancer. 53: 371. Available at: http://www.inchem.org/documents/iarc/vol53/15-pentachlorophenol.html. [May 4, 2006].

Innes, J.R.M., Ulland, B.M., Valerio, M.G., *et al*. 1969. Bioassay of pesticides and industrial chemicals for tumorigenicity in mice. A preliminary note. J. Natl. Cancer Inst. 42: 1101-1114. Cited In: U.S. EPA, 1993.

Johnson, R., Gehring, P., Kociba, R., and Schwetz, B. 1973. Chlorinated dibenzodioxins and Pentachlorophenol. Environ. Health Perspect. 5: 171-175. Cited In: CalEPA, 1997.

JW. 2005. Final Report. Environmental Site Assessment of CFB Gagetown, N.B: Task 2B- Stage 1 Development of a Strategic Approach. Report to: Public Works and Government Services Canada (PWGSC) on behalf of the Department of National Defence (DND). Project No. 1002588. Jacques Whitford, December 14, 2005

JW. 2006. Final Report. Task 2A: The History and Science of Herbicide Use at CFB Gagetown From 1952 to Present. Report to: Department of National Defence. Jacques Whitford, May 19, 2006.

Kerkvliet, N., Baecher-Steppan, L., and Schmitz, J. 1982. Immunotoxicity of pentachlorophenol. Toxicol. Appl. Pharmacol. 62: 55-64. Cited In: CalEPA, 1997.

Kimbrough, R., and Linder, R. 1978. The effect of technical and purified pentachlorophenol on the rat liver, Toxicol. Appl. Pharmacol. 46: 151-162. Cited In: CalEPA, 1997; ATSDR, 2001.

Knudsen, I., Verschueren, H., Den Tonkelaar, E., Kroes, R., and Helleman, P. 1974. Short-term toxicology of pentachlorophenol in rats Toxicology 2: 141-152. Cited In: CalEPA, 1997.

Larsen, R., Kirsch, L., Shaw, S., Christian, J., and Born, G. 1972. Excretion and tissue distribution of uniformly labelled 14C-pentachlorophenol in rats. J. Pharm. Sci. 61: 2004-2006. Cited In: CalEPA, 1997.

Larsson, P., Bremle, G., and Okla, L. 1993. Uptake of pentachlorophenol in fish of acidified and nonacidified lakes. Bull. Environ. Contam. Toxicol. 50:653-658. Cited In: U.S. EPA, 2004b.

Lyman, W.J., Reehl, W.F., and Rosenblatt, D.H. 1982. Handbook of Chemical Property Estimation Methods, Environmental Behavior of Organic Compounds. McGraw-Hill Book Co., New York, NY. Cited In: ATSDR, 2001.

Mecler, F.C. 1996. Pentachlorophenol: Fifty-two Week Repeated Dose Chronic Oral Study of Pentachlorophenol Administered *via* capsule to Dogs. Study conducted by TSI Mason Labs for the Pentachlorophenol Task Force (study no. 2-J31). Cited In: U.S. EPA, 2004a.

MEDITEXT®. 2006. TOMES® Information System Micromedex, Inc., Englewood, Co; CCIS Volume 128, expires May, 2006. Cited In: HSDB, 2005.

Nishimura, H., Nishimura, N., and Oshima, H. 1982. Effects of pentachlorophenol on the levels of hepatic glycogen. Japan. J. Indust. Health 24: 398-399. Cited In: CalEPA, 1997.

Norris, J.M. 1972. Acute Toxicological Properties of XD-8108.00L Antimicrobial. Studies conducted by Dow Chemical Co. Cited In: U.S. EPA, 2004a.

NTP. 1989. Technical Report on the Toxicology and Carcinogenesis Studies of Pentachlorophenol (CAS No. 87-86-5) in B6C3F1 mice (Feed Studies). National Toxicology Program Tech. Report No. 349. NIH Publ. No. 89-2804. Cited In: U.S. EPA, 1993.

Osheroff, M.R., *et al*. 1994. Ninety-one Day Repeated Dose Dermal Toxicity Study of Pentachlorophenol in Sprague-Dawley Rats. Study conducted by TSI Mason Labs for the Pentachlorophenol Task Force (study no. 2-J27). Cited In: U.S. EPA, 2004a.

PMRA. 2005. Re-evaluation Note: Update on the Re-evaluation of the Heavy Duty Wood Preservative. Pest Management Regulatory Agency. Available at: http://dsp-psd.pwgsc.gc.ca/Collection/H113-5-2005-3E.pdf#search='PMRA%20pentachlorophenol'. [September 6, 2006].

Reigner, B.G., *et al*. 1991. Pentachlorophenol toxicokinetics after intravenous and oral administration to rat. Xenobiotica 21(12): 1547-1558. Cited In: U.S. EPA, 2004a.

Reigner *et al*. 1992. Pharmaceut. Res. 9: 1053-1057. Cited In: U.S. EPA, 2004a.

Renner, G., Hopfer, C., and Gokel, J.M. 1986. Acute toxicities of pentachlorophenol, pentachloroanisole, tetrachlorohydroquinone, tetrachlorocatechol, tetrachlororesorcinol, tetrachlorodimethoxybenzenes and tetrachlorodibenzenediol diacetates administered to mice. Toxicol Environ Chem 11: 37-50. Cited In: ATSDR, 2001.

Rumack, B.H., and Hall, A.H (Eds.). 2006. POISINDEX® Information system Micromedex, Inc., Englewood, CO. CCIS Volume 128, expires May 2006. Cited In: HSDB, 2005.

Schmidt, J. 1992a. Aerobic Aquatic Metabolism of [carbon 14] Pentachlorophenol: Lab Project Number: 38354. Unpublished study prepared by ABC Labs, Inc. 38 p. Cited In: U.S. EPA, 2004b.

Schmidt, J. 1992c. Aerobic Soil Metabolism of (carbon 14)-Pentachlorophenol: Lab Project Number: 38353. Unpublished study prepared by ABC Labs, Inc. 41 p. Cited In: U.S. EPA, 2004b.

Schmidt, J. 1992b. Anaerobic Aquatic Metabolism of 14C-Pentachlorophenol: Lab Project Number: 38355. Unpublished study prepared by ABC Laboratories, Inc. 37 p. Cited In: U.S. EPA, 2004b.

Schwetz, B.A., Keeler, P.A., and Gehring, P.J. 1974. The effect of purified and commercial grade pentachlorophenol on rat embryonal and fetal development. Toxicol. Appl. Pharmacol 28: 151-161. Cited In: U.S. EPA, 2004a, CalEPA, 1997 and ATSDR, 2001.

Schwetz, B.A., Quast, J.F., Keelev, P.A., Humiston, C.G., and Kociba, R.J. 1978. Results of 2-year toxicity and reproduction studies on pentachlorophenol in rats. In: Rao, K.R. (Ed.). Pentachlorophenol: Chemistry, Pharmacology and Environmental Toxicology. Plenum Press, NY. p. 301. Cited In: U.S. EPA, 1993 and CalEPA, 1997.

Selim, S. 1985. Evaluation of the Dermal Absorption Characteristics of Pentachlorophenol. Unpublished study prepared by Biological Test Center. 18p. Cited In: U.S. EPA, 2004a.

St. Omer, V.E.V., and Gadusek F. 1987. The acute oral LD_{50} of technical pentachlorophenol in developing rats. Environ Toxicol Chem 6:147-149. Cited In: ATSDR, 2001.

U.S. EPA. 1979. Water-related environmental fate of 129 priority pollutants. Volume. 2. U.S. Environmental Protection Agency, Office of Water and Waste Management, Washington, DC. EPA 440/4-79-029B. Cited In: ATSDR, 2001.

U.S. EPA. 1993. Pentachlorophenol. Integrated Risk Information System, U.S. Environmental Protection Agency. Available at: http://www.epa.gov/iris/subst/0256.htm. [May 4, 2006].

U.S. EPA. 2000. U.S. EPA Toxicological Review of Pentachlorophenol (Cas No. 87-86-5) In Support of Summary Information on the Integrated Risk Information System (IRIS). U.S. Environmental Protection Agency. Available at: http://www.epa.gov/oppad001/pentachlorophenol.pdf#search='IRIS%20pentachlorophenol'. [September 7, 2006].

U.S. EPA. 2004a. PCP: Toxicology. U.S. Environmental States Protection Agency. Docket No. OPP-2004-0402.

U.S. EPA. 2004b. Pentachlorophenol: Ecological Effects and Risk Characterization. U.S. Environmental Protection Agency. Docket No. OPP-2004-0402.

U.S. EPA. 2004c. Pentachlorophenol: Human Exposure. U.S. Environmental Protection Agency. EPA-HQ-OPP-2004-0402-0006.

Verschueren K. 1983. Handbook of environmental data on organic chemicals 2nd Edition. Van Nostrand Reinhold Co., New York, NY, 953-954.

Weeden, D. 1993. Pentachlorophenol: Determination of the Sorption and Desorption Properties: Lab Project Number: 92-12-4536: 12836.0692.6113.710. Unpublished study prepared by Springborn Laboratories, Inc. 69 p. Cited In: U.S. EPA, 2004b.

Welsh, J.J., *et al*. 1987. Teratogenic potential of purified pentachlorophenol and pentachloroanisole in subchronically exposed sprague-dawley rats. Fd. Chem. Toxic. 25(2): 163-172. Cited In: U.S. EPA, 2004a.

Wester, R.C., *et al*. 1993. Percutaneous absorption of pentachlorophenol from soil. Fundam. Appl. Toxicol. 20: 68-71. Cited In: U.S. EPA, 2004a.