Australian Government
Department of Health and Aged Care
Australian Industrial Chemicals Introduction Scheme

Benzene, 1,2,3,4,5-pentachloro- (PeCB)

Evaluation statement

22 December 2022

Table of contents

Contents

AICIS evaluation statement

Subject of the evaluation

Benzene, 1,2,3,4,5-pentachloro- (PeCB)

Chemical in this evaluation

Name	CAS registry number
Benzene, 1,2,3,4,5-pentachloro-	608-93-5

Reason for the evaluation

Evaluation is needed to provide information on human health and environmental risks.

Parameters of evaluation

Pentachlorobenzene (PeCB) is currently listed on the Australian Inventory of Industrial Chemicals (the Inventory). PeCB was identified as a persistent organic pollutant (POP) at the fourth conference of parties to the *Stockholm Convention on Persistent Organic Pollutants* (the Stockholm Convention). The global use of PeCB as an industrial and agricultural chemical has been prohibited under the Stockholm Convention since 2009. Australia has not yet ratified the listing of PeCB on the Stockholm Convention; however, controls on the disposal of PeCB and management of PeCB waste have been implemented.

This evaluation assesses the risk to workers, public and the environment from any potential introduction and subsequent industrial use of the chemical and whether the risks can be managed within existing risk management frameworks.

Summary of evaluation

Summary of introduction, use and end use

The chemical (PeCB) is currently listed on the Inventory and may be introduced in Australia as a listed introduction under the *Industrial Chemicals Act, 2019 (IC Act).*

The chemical was widely used in the past; however, there is no information on the manufacture and importation volume of PeCB as a pure chemical or as a component in chemical products, or in imported articles. According to the industry, the manufacture of PeCB ceased in 1995 and its use in articles ceased in 1998 (Commonwealth of Australia 2009).

In Australia, PeCB was used historically as:

- a viscosity modifier in polychlorinated biphenyl (PCB) mixtures. PCBs were used as dielectric and coolant fluids in electrical apparatus such as transformers and capacitors
- flame retardant in plastics and textiles
- a chemical intermediate in the manufacture of other chemicals.

Articles produced or imported containing PeCB in the past are likely to remain in use and will be present in the environment for some time. PeCB is also unintentionally introduced through combustion of organic wastes, degradation of certain chlorinated compounds, and is also formed as a byproduct during the manufacture of some organochlorine chemicals.

The technical grade hexachlorobenzene (HCB; CAS No 118-74-1) contains a small proportion of PeCB (WHO-IPCS 1991). HCB is also present at low levels as an impurity in herbicides, pesticides and fungicides, which would result in diffuse releases of PeCB to the environment.

Human health

Summary of health hazards

The critical health effect for risk characterisation is acute toxicity following oral exposure. Effects on the liver, kidneys, and central nervous system (CNS) were reported in experimental animals exposed to high concentrations of PeCB. Repeated exposure to PeCB caused adverse effects on the liver and kidneys. Available data on the adverse effects of PeCB in humans are limited. Epidemiological studies that provide information on the adverse effects of exposed populations to PeCB are not available.

The chemical is not readily metabolised in most species, due to its high degree of chlorine substitution which in turn inhibits the formation of the arene-oxide intermediates, identified to be important in the metabolism of the less-chlorinated benzene derivatives (NTP 1991). Following an oral dose of PeCB in rodents, the chemical was found in the blood, liver, kidney, brain and fat tissue as well as in faeces (Umegaki et al. 1993). In coyotes, residues of PeCB were found in faeces and adipose tissue up to 6 months from oral dosing (UNEP 2007a). PeCB was detected in human breast milk (maximum of 1 µg/kg) and found to accumulate in human placenta (UNEP 2007a). The major urinary metabolites of PeCB included pentachlorophenol (PCP), 2,3,4,5-tetrachlorophenol (TCP), mercaptotetrachlorophenol (MTCP), and the glucuronide derivative of pentachlorothiophenol (PCTP) (Den Besten et al. 1994; Umegaki et al. 1993).

The chemical is acutely toxic by oral exposure with median lethal doses (LD50s) between 250 and 1125 mg/kg bw in rodents. Sublethal effects included decreased activity, tremors, narcosis, porphyria, enlarged kidneys, liver and adrenal glands, and increased in cytochrome P450 activity and hepatic enzyme levels (Government of Canada 1993; Linder et al. 1980; UNEP 2007a).

The chemical has low acute dermal toxicity with LD50 of >2500 mg/kg bw in rats. No adverse effects were reported in the study (Government of Canada 1993; Linder at al.1980; NTP 1991; UNEP 2007a).

There are no available studies on acute inhalation toxicity, skin and eye irritation potential, or skin sensitisation effect of the chemical.

Based on the available data, PeCB is potentially harmful following repeated oral exposure. In various subchronic oral toxicity studies, the liver and the kidneys are the primary target organs in rodents. In general, toxicity effects were more extensive in rats than in mice. Haematological findings and thyroid effects were also reported (Government of Canada 1993; NTP 1991; UNEP 2007a). In rats fed with diet containing PeCB for 100 days, the no observed adverse effect level (NOAEL) in females was 250 ppm (equivalent to 18.2 mg/kg bw/day) and the lowest observed effect level (LOAEL) in males was 125 ppm (equivalent to 8.3 mg/kg bw/day) based on hepatic and renal effects (Linder et al. 1980; UNEP 2007a). In a 13 week study, similar effects on the liver and kidneys were reported in Fischer 344 (F344) rats and B6C3F1 mice. Haematological effects in rats consistent with anaemia were reported. Functional effects on the thyroid were reported in both rats and mice. The NOAELs for histologic lesions were 33 ppm (approximately 2.4 mg/kg bw/day) for male rats and 330 ppm (24 mg/kg bw/day) for female rats. The NOAEL for female mice was 100 ppm (approximately 22 mg/kg bw/day). An NOAEL was not established for male mice (McDonald 1991; NTP 1991).

Based on limited available data, PeCB was not considered to be genotoxic. PeCB was not mutagenic in bacterial mutation assay with and without metabolic activation (S9) (Government of Canada 1993; NTP 1991). PeCB was also negative in Chinese hamster ovary cell assays for induction of sister chromatid exchanges and chromosomal aberrations (NTP 1991).

There is limited data on the carcinogenicity of PeCB. The available data are insufficient to determine whether the chemical has carcinogenic potential relevant to humans (Government of Canada 1993; NTP 1991).

The available data are insufficient to determine whether the chemical causes reproductive and developmental effects in humans. Several reproductive and developmental toxicity studies in animals showed adverse effects on foetal development. Tremors and mortality following oral exposures to high doses were also reported in rat offspring (Linder et al, 1980; NTP 1991). Histological examinations showed abnormal effects of various organs in rat weanlings fed up to 59 mg/kg bw/day for 28 days (Chu et al 1983; Government of Canada 1993; NTP 1991). In mice, no adverse effects were reported in offspring at maternally toxic doses (≥50 mg/kg bw/day) (Courtney et al. 1977; Government of Canada 1993; NTP 1991).

Hazard classifications relevant for worker health and safety

The chemical satisfies the criteria for classification according to the Globally Harmonised system of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant for work health and safety as follows. This does not consider classification of physical hazards and environmental hazards. This is the current classification on the Hazardous Chemicals Information System.

Health hazards	Hazard category	Hazard statement
Acute Toxicity – oral	Acute Tox. 4	H302: Harmful if swallowed

Summary of health risk

Public

The chemical is acutely toxic by oral exposure and has been shown to accumulate in adipose tissues in experimental animals. The liver and kidneys are major target organs following acute and subchronic oral exposures to PeCB.

There is a global phase out of manufacture and use of PeCB; therefore, public exposure from use of articles containing PeCB is expected to decline to minimal levels as the articles reach the end of their useful life. Introduction by manufacture or import, and the subsequent use of PeCB could increase the risk to the public based on the health effects and potential for exposure, including secondary exposure from their environment.

The proposed means of managing risks to the environment would also minimise risk to the public (see **Proposed means for managing risks**).

Workers

The major route of occupational exposure is expected to be due to release of the chemical from articles. Articles containing PeCB are no longer imported into Australia. Occupational exposure from use of articles is expected to decline to minimal levels due to the global phase-out of PeCB.

Introduction by manufacture or import, and the subsequent use of PeCB could increase the risk to the workers based on the critical health effects and potential for exposure, including secondary exposure from their environment.

The proposed means of managing risks to the environment would also minimise risk to the workers (see **Proposed means for managing risks**).

Environment

Summary of environmental hazard characteristics

The chemical is a POP as defined by the Stockholm Convention. The Stockholm Convention Technical Review Committee has agreed that the chemical meets the POP criteria in Annex D for:

- Persistence
- Bioaccumulation
- Potential for long range environmental transport (LRT)
- Adverse effects.

Environmental hazard classification

The chemical satisfies the criteria to be classified for environmental hazards under the Globally Harmonised System of Classification and Labelling of Chemicals (GHS) (UNECE 2017) for hazard classes relevant to the environment as follows. This does not consider classification of physical hazards and human health hazards. These are the current

classifications listed in the Hazardous Chemical Information System (HCIS) (Safe Work Australia).

Environmental Hazard	Hazard Category	Hazard Statement
Acute Aquatic	Acute aq. – Cat. 1	H400: Very toxic to aquatic life
Chronic Aquatic	Chronic aq. – Cat. 1	H410: Very toxic to aquatic life with long lasting effects

Summary of environmental risk

PeCB is a POP chemical and has been listed under Annexes A and C of the Stockholm Convention, for global elimination from production and use. POP chemicals are persistent, bioaccumulative, cause adverse effects to animal life in the environment or humans, and undergo long range transport to remote regions of the world. Since the chemical is a POP, there are very significant long term risks to the environment from the manufacture, import and use of the chemical, including from introduction in articles.

No information on current introduction (import or manufacture), use and end use of the chemical have been identified. According to industry, the manufacture of the chemical has ceased in 1995 and the use as component of articles ceased in 1998. The inclusion of PeCB in Annex A does not prevent the chemical being introduced as a manufacturing impurity. The chemical has been identified as an impurity in HCB. The risks from the introduction and subsequent use of HCB are the subject of another evaluation.

Introductions authorised as a listed introduction

Since PeCB is currently listed on the Inventory it may be introduced in Australia as a listed introduction under the *Industrial Chemicals Act 2019 (IC Act).* Any introduction of the chemical into Australia would increase the already significant risks identified from past environmental exposure to PeCB. Advice on the existing risk management framework was sought from the Department of Climate Change, Energy, the Environment and Water (DCCEEW). There are current restrictions in place under the National Strategy for Management of Scheduled Waste on the disposal of chemical residues and treatment of waste articles containing PeCB. However, DCCEEW advised that the risks to the environment posed by the introduction and use of the chemical cannot be managed within the current risk management framework. The current risk management framework cannot eliminate the introduction (import and manufacture) and use of the chemical.

Historical introductions and presence in articles

The chemical is likely to be present in Australia in articles produced and imported in the past, or in environmental compartments as a result of its historical use. The release to the environment from these sources requires supplementary risk management controls. This risk could be managed through development of nationally consistent controls through the *Industrial Chemicals Environment Management Standard (IChEMS) 2021* on introduction, use and disposal of the chemical, that extends to imported articles containing PeCB.

Proposed means for managing risks

Inventory listing

The Executive Director is not satisfied that the environmental risks identified in this Evaluation Statement can be managed. Therefore, the Inventory listing for benzene, 1,2,3,4,5-pentachloro- (PeCB; CAS No. 608-93-5) should be removed under *Section 95* of the *Industrial Chemicals Act 2019*.

Environment

Recommendation to Department of Climate Change, Energy, the Environment and Water (DCCEEW)

The chemical is recommended for environment scheduling as a high risk chemical, with prohibitions, restrictions and risk management measures attached that will minimise further release to the environment from introductions as a manufacturing impurity, historical introductions of PeCB and imported articles containing PeCB.

Conclusions

The conclusions of this evaluation are based on the information described in this Evaluation Statement.

PeCB is a POP chemical and has been listed under Annexes A and C of the Stockholm Convention, for global elimination from production and use. Australia is a Party to the Stockholm Convention. Under Article 3.1 of the Stockholm Convention, Australia is committed to manage chemicals listed under Annex A in accordance with the requirements of the Stockholm Convention to eliminate production and use of these chemicals.

Considering the human health and environmental effects of PeCB and its fate in the environment identified in this Evaluation Statement, there are risks to the environment and potential risks to public and workers via secondary exposure from the environment, through introduction by import or manufacture, and the subsequent use of the chemical.

Taking into consideration advice from DCCEEW that the environmental risks from the introduction and subsequent use of PeCB cannot be managed within the current risk management framework, the Executive Director is not satisfied that environmental risks identified in this Evaluation Statement, can be managed. Therefore, under *Section 95* of the *IC Act*, the chemical may be removed from the Inventory listing by the Executive Director (see **Proposed means of managing risks**). This means of managing risks would also minimise any potential risks to public and workers via secondary exposure from the environment.

PeCB is likely to be present in Australia in articles produced and imported in the past, or in environmental compartments as a result of its historical use. Since, PeCB has the hazard characteristics of a POP, there are potential risks to the environment from these sources. Therefore, release to the environment from these sources require supplementary risk management controls (see **Proposed means of managing risks**).

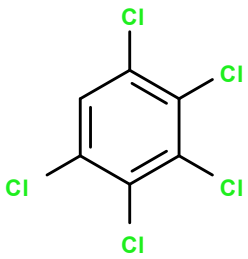
Supporting information

Rationale

The chemical, PeCB, was identified as a persistent organic pollutant (POP) at the fourth conference of parties to the Stockholm Convention. Its global use as an industrial and agricultural chemical has been banned under the Stockholm Convention since 2009. Australia has not yet ratified the chemical listing of PeCB on the Stockholm Convention; however, controls on disposal of PeCB waste have been implemented. As a result of the listing, industry use and manufacture of the chemical in Australia was discontinued in 1998 (Commonwealth of Australia 2009).

No current industrial use of the chemical in Australia has been identified and the use of the chemical is prohibited globally. However, since PeCB is currently listed on the Inventory under the *Industrial Chemicals Act, 2019* there are no current restrictions on the importation, manufacture or use of the chemical in Australia. This evaluation will assess the risk of introduction by manufacture or import and subsequent use of PeCB and make appropriate recommendations to manage the risk of the chemical.

Chemical identity

Chemical Name	Benzene, 1,2,3,4,5-pentachloro-
CAS RN	608-93-5
Synonyms	PeCB pentachlorobenzene quintochlorobenzene
Structural formula	
Molecular formula	C_6HCl_5
Molecular weight (g/mol)	250.3 g/mol
SMILES	c(c(c(c(c1Cl)Cl)Cl)Cl)(c1)Cl
Chemical description	Chlorinated aromatic compound

Relevant physical and chemical properties

Physical form	White crystalline solid with characteristic odour
Melting point	86 °C
Boiling point	277 °C
Vapour pressure	0.2667 Pa at 25 °C
Water solubility	0.56 mg/L at 20 °C
Henry's law constant	71.9 Pa·m^3/mol at 20 °C
Ionisable in the environment?	No
pKa	-
log K_{OW}	5.18

PeCB is a crystalline solid, slightly soluble in water and moderately volatile. The Henry's law constant of PeCB suggests moderate volatility from water. A logarithmic octanol-water partition coefficient (log K_{OW}) greater than 4.2 indicates that the chemical is highly lipophilic.

Introduction and use

Australia

No information on current introduction (import or manufacture), use and end use of PeCB have been identified.

The chemical was historically manufactured and used in Australia, although no information on volumes produced are available. According to industry, the manufacture of the chemical has ceased in 1995 and the use as component of articles ceased in 1998 (Commonwealth of Australia 2009).

The chemical was historically used as a viscosity modifier in polychlorobiphenyl (PCB) mixtures. PCBs were used as dielectric and coolant fluids in electrical apparatus such as transformers and capacitors. PeCB was also used as a flame retardant and as an intermediate in the manufacture of other chemicals.

The chemical also had non-industrial uses as a chemical intermediate for the production of the fungicide pentachloronitrobenzene (quintozene, CAS RN 82-68-8), and as a wood preservative (UNEP, 2007a).

Technical grade HCB contains approximately 98% HCB, 1.8% PeCB and 0.2% 1,2,4,5-tetracholorobenzene (WHO-IPCS 1991). HCB was found as an impurity in herbicides, pesticides and fungicides, which could also be a minor source of PeCB.

International

PeCB is no longer manufactured globally and has no commercial uses (UNEP, 2007a).

The chemical was used as a dyestuff carrier in the textile industry (UNEP, 2007a).

The chemical was also found as an impurity in various herbicides, pesticides and fungicides (UNEP 2007a).

Existing Australian regulatory controls

AICIS

No specific controls are currently available for the chemical.

Public

No specific controls are currently available for the chemical.

Workers

The chemical is currently listed on the Hazardous Chemical Information System HCIS (SWA) with the following health hazard category and statements:

Health hazards	Hazard category	Hazard statement
Acute Toxicity – oral	Acute Tox. 4	H302: Harmful if swallowed

No exposure standards are available for the chemical in Australia (SWA).

Environment

PECB was identified as a chemical of concern in the proposed national strategy for management of scheduled wastes (ANZECC 1992). Public awareness of its environmental risks led to the regulation of its disposal under various state legislation (ACT 2000; Queensland 2019; South Australia 2015). Restrictions in place on the disposal of chemical residues and treatment of waste articles containing PeCB are outlined in the National Strategy for Management of Scheduled Wastes. To date, only NSW has prohibited the use and production of PeCB (NSW EPA 2004).

To ratify the listing in the Stockholm Convention, Australia must undertake a domestic treaty making process. DCCEEW works to ensure that newly-listed POPs are being managed across Australia in accordance with the requirements of the Stockholm Convention. Once these POPs are being managed as required, the Government can decide whether to ratify the new listings. Industrial chemicals such as PeCB that are listed under the Stockholm Convention but not yet ratified by Australia are a priority for IChEMS scheduling.

International regulatory status

United Nations

The chemical is listed as a POP under Annex A (elimination) and Annex C (unintentional production) of the Stockholm Convention (UNEP 2001). The listing prohibits production and use of the chemical and member countries must take efforts to reduce the unintentional production of this chemical that may occur in the preparation of other chemicals products.

Canada

The chemical is listed under Schedule 1 (the Toxic Substances List) of the Canadian Environmental Protection Act 1999 (CEPA 1999) (Government of Canada 1999).

The chemical is subject to and listed under the *Prohibition of Certain Toxic Substances Regulations, 2012* (Government of Canada 2012), that prohibits the manufacture, use, sale, offer for sale or import of certain toxic substances and products containing these substances with a limited number of exemptions. Canada has nominated PeCB for Annex I of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade.

European Union

The chemical is subject to the European Chemicals Agency (ECHA) substance regulatory obligations whilst listed under Annex A and C of the Stockholm Convention (ECHA). The chemical is also listed on the *European Commission's POP Regulation (Regulation (EU) 2019/1021) in Annexes I, III and IV*. The chemical is subject to prohibition, release reduction and waste management provisions in the member states of the European Union (ECHA).

Asia

The chemical is listed in Japan under Class I – Substances that are persistent, are highly bioaccumulative, and have a risk of long-term toxicity to humans or predator animals at higher trophic level (NITE). Prior permission is required before manufacture or import of the chemical, and use is prohibited except for essential uses.

Health hazard information

Toxicokinetics

Following a single oral dose (15 or 20 mg/kg bwF) in rats for 15 days, PeCB was distributed in the blood and tissues (Umegaki et al. 1993). In rats treated with 40-250 mg/kg of PeCB (route unspecified) for 5 days, the highest concentration of the chemical was found in the fat and lower concentrations were detected in the liver, kidney, and brain (Umegaki and Ichikawa 1988). In rats fed diets containing PeCB (125 or 1000 ppm for 100 days in males and 125, 250, 500 or 1000 ppm for 180 days in females), approximately 1.5 to 2.2 times the dietary concentration of PeCB had accumulated in the adipose tissues (Linder et al. 1980).

After a single oral administration of 15 or 20 mg/kg bw PeCB (intragastric), the metabolism of PeCB in young rats was at a much higher rate than in adult rats. The biological half life of

PeCB in the blood was 10.6 hours in young rats and 42.9 hours in adult rats. This mechanism was reported to be associated with the differences in fat tissue mass where a smaller fat tissue mass enhanced the concentration of PeCB in the liver, resulting in faster metabolism through hepatic drug metabolising enzymes and subsequent excretion (Umegaki et al. 1993).

After a 13 week dietary study (0.03% and 0.13% PeCB) in female Wistar rats, PeCB was oxidised to form the metabolites pentachlorophenol (PCP) and tetrachlorohydroquinone (TCHQ). The major urinary metabolites included 2,3,4,5- tetrachlorophenol (TCP), mercaptotetrachloro-phenol (MTCP), and the glucuronide derivative of pentachlorothiophenol (PCTP) (Den Besten et al. 1994; Umegaki et al. 1993).

In a single oral study in coyotes (3 animals /dose) treated with 130, 260 or 520 mg/kg bw PeCB, the chemical was excreted in the faeces and was detectable in faeces for 6 months post treatment. In the faeces, the metabolites found were PCP and TCP (UNEP 2007a).

The chemical was detected in breast milk and found to accumulate in human placenta (Shen et al. 2007). The mean concentration of PeCB in the breast milk of Canadian women taken 3 to 4 weeks after parturition was a maximum of 1 µg/kg. In this Canadian survey, PeCB was detected in 97% of the 210 samples analysed (detection limit and sampling period unspecified) (Government of Canada 1993). Similarly, "trace" (<1 µg/kg) amounts of PeCB in breast milk were detected in samples from Canadian indigenous population (Government of Canada 1993). Two other studies investigating PeCB in human milk reported concentrations in the range of 1 to 5 µg/kg (WHO-IPCS 1991). PeCB was present in abdominal, mammary, and perirenal fat tissue of 27 adult Finnish males and females (UNEP 2007a).

Acute toxicity

Oral

There are sufficient data to indicate that PeCB is acutely toxic by oral administration. The current hazard classification ‘Acute toxicity – Category 4’ (Harmful if swallowed) is appropriate (SWA).

In an acute oral toxicity study, Sherman rats (10/dose, mixed sex) were treated with a single dose of the chemical. The median lethal doses (LD50s) were 1125 and 1080 mg/kg bw for males and females, respectively. Weanling Sherman rats (10/dose, female, 27-35 days of age) treated with a single dose of PeCB had an oral LD50 of 940 mg/kg bw. Reported sublethal signs of toxicity across all animals included tremor, decreased activity, hypersensitivity to touch, red staining of the mouth, nose, and eyes, weakness, and laboured breathing (Government of Canada 1993; Linder at al.1980; NTP 1991; UNEP 2007a).

As part of the study above (Linder et al. 1980), Swiss Webster mice (10/dose, mixed sex) were also treated with a single dose of the chemical. The oral LD50s were 1175 and 1370 mg/kg bw for male and female animals, respectively. Reported sublethal signs of toxicity included tremor, decreased activity, and hypersensitivity to touch.

An oral LD50 of 250 mg/kg bw was reported in rats. No other information was provided for the study (NTP 1991).

Dermal

In an acute dermal toxicity study, 2500 mg/kg bw PeCB was applied to shaved skin of Sherman rats (number not reported, mixed sex) and observed for 14 days (Linder et al. 1980). No signs of toxicity were observed in either sex during the observation period.

Inhalation

No data were available for the chemical.

Irritation/Sensitisation

No studies were available for the chemical

Repeat dose toxicity

Oral

Subchronic

In a non-guideline study, F344/N rats (5/sex/dose) were administered the chemical in feed at 0, 100, 330, 1000, 3300, or 10000 ppm for 15 days. All animals at the highest dose (10000 ppm) died (males by day 7 and females by day 6, respectively). No mortality was reported at doses below the highest dose. Oral doses at 3300 ppm caused significant body weight loss in both sexes. Centrilobular hypertrophy in the liver was reported in all females at 3300ppm and at ≥ 1000 ppm in all males. Hyaline droplets were reported in males from 100 ppm and above (McDonald 1991; NTP 1991).

As part of the same study above, B6C3F_1 mice (5/sex/dose) were administered the chemical in feed at 0, 100, 330, 1000, 3300 or 10 000 ppm for 15 days. All male and female mice that received 3300 or 10 000 ppm, died by day 15. Tremors, lethargy, hunched posture, dyspnoea, paralysis at 3300 ppm. At 330 or 1000 ppm increased in liver weights; and at 3300 or 10 000 ppm, abnormalities in thymic lymphocytes and macrophages were observed (McDonald 1991; NTP 1991).

In a non-guideline study, Sherman rats (10/sex/dose) were fed 0, 125, 250, 500 or 1000 ppm PeCB for 180 days in female, and 0, 125 or 1000 ppm PeCB for 100 days in males. A dose dependent increase in the accumulation of PeCB in adipose tissue was reported in both sexes. Decreased red blood cells and heamatocrit in males, and decreased haemoglobin in both sexes were reported at 1000 ppm (equivalent to 81.1 mg/kg bw/day for males and 78.7 mg/kg bw/day in females). Hepatocellular enlargement and hypertrophy of hepatic cells were reported in females at ≥500 ppm (equivalent to ≥37.5 mg/kg bw/day) and in males at 1000 ppm. Increase in adrenal weight, dilated renal tubules with eosinophilic materials and epithelial cells containing hyaline droplets (dose dependent) were reported in males at ≥125 ppm (≥8.3 mg/kg bw/day). In males, the presence of foci in the renal cortex consisting of atropic tubules and interstitial lymphocytic infiltration was reported. The study concluded that the hepatic and renal effects were associated with some degree of cumulative toxicity (Linder et al. 1980). The NOAEL in female rats was 250 ppm (equivalent to 18.2 mg/kg bw/day) and the lowest observed adverse effect level (LOAEL) in males was 125 ppm (equivalent to 8.3 mg/kg bw/day) (UNEP 2007a).

In a dietary study, F344/N rats (20/sex/dose) were administered PeCB in feed at 0, 33, 100, 330, 1000 or 2000 ppm for 13 weeks. Observations in the kidney and liver, and haematologic effects similar to those in previously reported study were reported in rats. Centrilobular hepatocellular hypertrophy, yellow brown pigment granules in hepatocytes and renal tubular epithelium were reported. The granules may have contained porphyrins. Minimal thyroid follicular cell hypertrophy was present. Significant decrease in free and total thyroxine (T4) concentrations indicating moderate hypothyroxinemia were reported. Haematological findings were consistent with anaemia that is microcytic (decreased mean cell volume), hypochromic (decreased mean corpuscular haemoglobin concentration, females), and poorly regenerative (slight to no change in reticulocyte counts). The NAOELs for histologic lesions were 33 ppm and 330 ppm for male and female rats, respectively (approximately 2.4 and 24 mg/kg bw/day, respectively). In the same study, mice (20/sex/dose) were fed 0, 33, 100, 330, 1000 or 2000 ppm PeCB for 13 weeks. No compound related deaths occurred. Histological lesions found in mice were centrilobular hepatocellular hypertrophy (both sexes) and hepatocellular necrosis (at all concentrations in males). Other effects observed at various concentrations included ventral swelling and ruffled fur (highest dose tested), increased kidney weights, decreased T4 concentrations and increased liver weights. The NOAEL based on histologic lesions in female mice was 100 ppm (approximately 22 mg/kg bw/day). An NOAEL was not established for male mice (McDonald 1991; NTP 1991).

In a non-guideline study (Chu et al. 1983; Government of Canada 1993; NTP 1991), weanling Sprague Dawley (SD) rats (10/sex/dose) were administered PeCB in feed at 5, 50 or 500 ppm for 28 days (equivalent to 0.55, 7.8 or 71 mg/kg bw/day in males and 0.59, 6 or 59 mg/kg bw/day in females). No clinical signs of toxicity were observed. Liver weight was increased in females receiving 500 ppm (males not reported). Serum sorbitol dehydrogenase activity was increased in male rats receiving 500 ppm. Liver aniline hydroxylase activity was increased in male rats receiving 50 or 500 ppm. Histological lesions were reported in the liver, thyroid, and kidneys of all treated groups except in males dosed at 5 ppm.

Dermal

No studies are available for the chemical.

Inhalation

No studies are available for the chemical

Observation in humans

Epidemiological studies of populations exposed to PeCB, or reports of adverse effects in individuals following exposure to PeCB have not been identified (Government of Canada 1993).

Genotoxicity

The chemical was reported not to be mutagenic in gene mutation assay conducted in *Salmonella typhimurium* with and without S9 (Government of Canada 1993; NTP 1991). The chemical was also reported to be negative in Chinese hamster ovary cells in in vitro assays for induction of sister chromatid exchanges and chromosomal aberrations (NTP 1991). No increase in micronuclei were reported from peripheral blood smears in animals orally exposed to PeCB for 13 weeks (NTP 1991).

Carcinogenicity

Data on the carcinogenicity of PeCB in animals were not available. Several medium term carcinogenicity assays (NTP 1991; UNEP 2007a) investigated the tumour promoting activity of various chlorobenzene isomers including PeCB. PeCB was found to promote glutathione S-transferase (GSTP1-1) positive preneoplastic foci formation in rat liver, following diethylnitrosamine (DEN) initiation (UNEP 2007a).

Health Canada and USEPA reviewed the potential for PeCB to cause cancer and concluded that PeCB is not classified as a carcinogen (UNEP 2007a).

Reproductive and development toxicity

The chemical was shown to cross the placental barrier and accumulate in foetal tissues in rats and other species. Weanling rats (10/sex) were fed diets at 0, 125, 250, 500 and 1000 ppm (females) and 0, 125 and 1000 ppm (males) for 67 days. Both males and females were pair bred with previously untreated partners. Females were treated throughout breeding, gestation and lactation. Suckling pups from dams orally treated with ≥250 mg/kg bw/day developed tremors (LOAEL equivalent to 18.2 mg/kg bw/day) and most pups died at 1000 ppm before weaning (Linder et al 1980; NTP 1991).

Pregnant Wistar rats were given oral doses of 50, 100 or 200 mg/kg bw/day PeCB on days 6-15 of gestation. Developmental effects (increased incidence of extra ribs and sternal defects) were reported in foetuses at maternal exposure of 50 mg/kg bw/day, below the concentration which induced maternal toxic effects in this study. At 200 mg/kg bw/day, decreased mean number of live foetuses/litter and mean foetal weight were reported. There were also higher incidences of supernumerary ribs and unossified or nonaligned sternebrae in offspring (Government of Canada 1993; UNEP 2007a).

Pregnant CD1 mice were administered PeCB by gavage at 50, 100 or 200 mg/kg bw/day on gestation days 6-15. No embryotoxic, foetotoxic or teratogenic effects were observed in the offspring at maternally toxic doses (50 mg/kg bw/day and above) (Courtney et al. 1977; Government of Canada 1993; NTP 1991).

Environmental exposure

The chemical may be present as an unintended impurity in a number of industrial chemical products. The chemical is a known impurity in a number of agricultural pesticides currently on the market; however, no industrial products with PeCB as an impurity have been identified. Given that some herbicides, pesticides and fungicides contain HCB as an impurity, such agricultural products could also be a minor source of PeCB.

Releases of PeCB to the environment are expected to continue as a result of its historical use. These releases are expected from the following:

- direct emissions to air from the incomplete combustion of solid organic wastes in open landfills and municipal incinerators
- diffuse source emissions from old electrical equipment and products that contain this chemical

- diffuse emissions from agricultural fields that result from either PeCB impurities present in the applied pesticides or from degradation of legacy hexachlorobenzene (CAS RN 118-74-1), quintozene and other chlorinated pesticides.

Other processes that may result in minor emissions of PeCB include ore treatment for the production of magnesium and some other metals, and from the use of chlorinated solvents in industries and laboratories (UNEP 2007a).

Environmental fate

Partitioning

Most releases to the environment go directly into the air phase. Given its volatile properties, PeCB is expected to be present mainly as vapour in the atmosphere, with limited partitioning to aerosols and airborne particles.

The chemical volatilises from water under normal atmospheric conditions, as indicated by a Henry's Law value of 71.9 $Pa \cdot m^3/mol$. However, volatilisation from wet soil may be hindered by strong adsorption to organic matter (log Koc = 4.77). In soil, PeCB is expected to be largely immobile. Fugacity modelling assuming equal emission to all compartments (level III approach) suggests a distribution of 2.4% to air, 4.7% to water, 92.2% to soil and 0.7% to sediment under steady-state conditions (US EPA 2017).

Degradation

The chemical is reported to be persistent in air, water, soil and sediment phases.

Half lives in the air phase are estimated between 155 days by photodegradation and 277 days by reaction with hydroxyl radicals (UNEP 2007a).

In surface waters, overall estimated half lives are 194−1250 days, although PeCB can be photodegraded to some extent. In deep anaerobic waters, half lives are reported at 776-1380 days in the water phase and 187−1550 days in sludge-sediment (UNEP 2007a; Wang and Jones 1994). Only one bacterial strain is known to degrade chlorobenzenes (Adrian and Görisch 2002).

The chemical is not degraded in aerobic soils, where half lives are estimated between 260 and 7300 days (UNEP 2007a).

Bioaccumulation

The chemical is highly lipophilic (log Kow 5.18) and bioaccumulates in tissues of organisms.

Measured bioconcentration factors (BCF) in aquatic organisms range from 1085–23 000 L/kg for fish; 833–4300 L/kg for molluscs, and 577–2258 L/kg for crustaceans (UNEP 2007a). Since PeCB partitions to organic matter, a major route of exposure in aquatic organisms is through ingestion of contaminated food sources.

Bioaccumulation of PeCB is demonstrated by the numerous monitoring data existing in biota from temperate zones (mussels, seagulls, seals) and remote polar regions alike (mosses, fish, ptarmigans, penguins, musk oxen, Arctic foxes, polar bears and beluga whales) (Bailey

et al. 2009; UNEP 2007a; Vorkamp et al. 2004). PeCB is found mainly in the blood, liver, kidney, brain and fat tissues of animals, and also in their faeces. A major metabolite in animals is pentachlorophenol (CAS RN 87-86-5) (Umegaki et al. 1993), which is also a POP listed on the Stockholm Convention.

Environmental transport

Atmospheric long range transport of PeCB has been demonstrated both by monitoring and modelling (UNEP 2007a).

Monitoring data from North America indicate that PeCB travels long distances through air, where it has a long residence time. Relatively constant air concentrations suggests that PeCB is widely distributed in the global atmosphere (Shen et al. 2005). PeCB has been reported in air, precipitation, soil and sediments at various locations in the world far from its sources, as well as in abiotic (water, soil) and biotic (fishes, birds, mammals) matrices in remote polar regions of the Arctic and Antarctica (Bailey et al. 2009).

In general, concentrations of PeCB in sediment cores and biotic matrices of the temperate zones of the world show a decreasing trend, consistent with a reduction in emissions in developed countries (Bailey et al. 2009; UNEP 2007a).

Predicted environmental concentration (PEC)

No PEC is estimated, given that PeCB is no longer used in Australia and any releases to the environment from previous uses cannot be determined.

Environmental effects

Effects on Aquatic Life

The chemical is highly toxic to aquatic organisms.

Acute toxicity

The following measured median lethal concentration (LC50) and median effective concentration (EC50) values for aquatic organisms across 3 trophic levels were retrieved from the dossier of the Persistent Organic Pollutants Review Committee on this chemical (UNEP 2007b):

Taxon	Endpoint	Method
Fish	96 h LC50 = 0.250 mg/L	*Lepomis macrochirus* (Bluegill)
Invertebrate	48 h LC50 = 0.300 mg/L	*Daphnia magna* (waterflea)
Algae	96 h $EC50_{growth}$ = 6.63 mg/L*	*Selenastrum capricornutum* (freshwater algae)

* Value above the solubility limit

Chronic toxicity

The following no observed effective concentration (NOEC) values for aquatic organisms across 2 trophic levels were retrieved from the dossier of the Persistent Organic Pollutants Review Committee on this chemical (UNEP 2007b):

Taxon	Endpoint	Method
Fish	42 d $NOEC_{growth}$ = 0.002 mg/L	*Gambusia affinis* (Mosquito fish)
Invertebrates	21 d $NOEC_{reproduction}$ = 0.010 mg/L	*Daphnia magna* (waterflea)

Effects on sediment dwelling life

The chemical is highly toxic to sediment insect larvae, with 48 h LC50 = 0.23 mg/L for the midge *Chironomus thummi* (UNEP 2007b).

Effects on terrestrial Life

The chemical is toxic to plants, with 14 day growth $EC50_{growth}$ = 56 mg/kg dry weight for lettuce (*Lactuca sativa*) (Hulzebos, et al. 1993), and is slightly toxic to earthworms, with 14 day LC50 = 115 mg/kg dry soil for *Lumbricus rubellus* (van Gestel et al. 1991).

Endocrine effects/activity

The chemical was reported not to show endocrine activity (UNEP 2007a).

Predicted no-effect concentration (PNEC)

A PNEC has not been calculated as an acceptable toxicity threshold for persistent organic pollutants cannot be determined with any degree of certainty.

Categorisation of environmental hazard

The environmental hazards of PeCB were assessed by the international Review Committee of the Stockholm Convention on Persistent Organic Pollutants, which concluded the chemical is a POP.

Based on the information reviewed in this evaluation, PeCB meets the criteria of a POP according to the criteria in Annex D of the StockholmConvention:

Persistence

Based on measured data from degradation studies in air, water and sediment, PeCB meets the Annex D criteria for persistence.

Bioaccumulation

Based on high measured bioconcentration factors (BCF) in fish, a log K_{OW} value above the threshold of 5.0, and slow biotransformation in organisms, PeCB meets the Annex D criteria for bioaccumulation.

Adverse effects

Based on available ecotoxicity values in aquatic organism and evidence of high chronic toxicity, PeCB meets the Annex D criteria for adverse effects.

Potential for long range environmental transport (LRT)

Based on evidence of monitoring data showing that long range atmospheric transport of the chemical to a receiving environment, PeCB meets the Annex D criteria for LRT.

GHS classification of environmental hazard

The chemical is currently listed on the Hazardous Chemical Information System HCIS (SWA) with the following environmental hazard category and statements:

Environmental Hazard	Hazard Category	Hazard Statement
Acute Aquatic	Acute aq. – Cat. 1	H400: Very toxic to aquatic life
Chronic Aquatic	Chronic aq. – Cat. 1	H410: Very toxic to aquatic life with long lasting effects

References

AICIS ACT (Australian Capital Territory Government) (2000) *ACT's Environmental Standards: Assessment & Classification of Liquid & Non-liquid Wastes*, ACT, accessed May 2022.

Adrian L and Görisch H (2002) 'Microbial transformation of chlorinated benzenes under anaerobic conditions', *Research in Microbiology*, 153(3):131-137, doi:10.1016/S0923-2508(02)01298-6

ANZECC (Australian and New Zealand Environment and Conservation Council) (1992) *National Strategy for the Management of Scheduled Waste,* ANZECC, accessed May 2022.

Bailey RE, van Wijk D and Thomas PC (2009) 'Sources and prevalence of pentachlorobenzene in the environment', *Chemosphere*, 75(5):555-564, doi:10.1016/j.chemosphere.2009.01.038

Chu I, Villeneuve D, Secours V and Valli VE (1983) 'Comparative toxicity of 1,2,3,4-, 1,2,4,5-, and 1,2,3,5-tetrachlorobenzene in the rat: Results of acute and subacute studies', *Journal of Toxicology and Environmental Health*, 11(4-6):663-677, doi:10.1080/15287398309530375

Commonwealth of Australia (2009) *Regulation Impact Statement for the Consideration of the Addition of Nine Chemicals to the Stockholm Convention bn Persistent Organic Pollutants*, Commonwealth of Australia, accessed May 2022.

Courtney KD, Andrews JE and Ebron MT (1977) 'Teratology study of pentachlorobenzene in mice: no teratogenic effect at 50 or 100 mg/kg/day from day 6 to day 15 of gestation', *IRCS medical science. Library compendium*, 5:587.

Den Besten C, Bennik MMH, Van Iersel M, Peters MAW, Teunis C, and van Bladeren PJ (1994) 'Comparison of the urinary metabolite profiles of hexachlorobenzene and pentachlorobenzene in the rat', *Chemico-Biological Interactions*, 90:121–137, doi:10.1016/0009-2797(94)90098-1

ECHA (European Chemicals Agency) (n.d.) *List of substances subject to POPs Regulation - Pentachlorobenzene*, ECHA, accessed December 2021.

Government of Canada (1993) *Canadian Environmental Protection Act, Priority Substances List Assessment Report - Pentachlorobenzene*, Government of Canada, accessed November 2021.

Government of Canada (1999) *Canadian Environmental Protection Act, Toxic Substance List - Schedule 1*, Government of Canada, accessed November 2021.

Government of Canada (2012) *Prohibition of Certain Toxic Substances Regulations, 2012*, Government of Canada, accessed May 2022.

Hulzebos EM, Dirven-Van Breemen EM, van Dis WA, Herbold HA, Hoekstra JA, Baerselman R, van Gestel CAM, Adema DMM and Henzen L (1993) 'Phytotoxicity studies with Lactuca sativa in soil and nutrient solution', *Environmental Toxicology and Chemistry*, 12(6):1079-1094, doi: 10.1002/etc.5620120614

Linder R, Scotti T, Goldstein J, McElroy K and Walsh D (1980) 'Acute and subchronic toxicity of pentachlorobenzene', *Journal of Environmental Pathology and Toxicology,* 4(5-6):183-196.

McDonald (1991) 'NTP technical report on the toxicity studies of Pentachlorobenzene in F344/N Rats and B6C3F1 Mice (Feed Studies) (CAS No. 608-93-5)', *Toxicity Report Series* 6:1-48.

NITE (National Institute of Technology and Evaluation) (n.d.) *Pentachlorobenzene*, NITE, accessed October 2021.

NSW EPA (New South Wales Environment Protection Authority) (2004) *Scheduled Chemical Wastes Chemical Control Order 2004*, NSW EPA, accessed May 2022.

NTP (National Toxicology Program) (1991) *NTP report on the toxicity studies of Pentachlorobenzene in F344 rats and B6C3F1 mice (feed studies). NTP Tox 6* NTP, accessed May 2022.

Queensland (Government of Queensland) (2019) *Environmental Protection Regulation 2019*, Queensland, accessed May 2022.

Shen H, Main KM, Virtanen HE, Damggard IN, Haavisto AM, Kaleva M, Boisen KA, Schmidt IM, Chellakooty M, Skakkebaek NE, Toppari J and Schramm KW (2007) 'From mother to child: Investigation of prenatal and postnatal exposure to persistent bioaccumulating toxicants using breast milk and placenta biomonitoring', *Chemosphere*, 67(9):S256-62, doi: 10.1016/j.chemosphere.2006.05.106

Shen L, Wania F, Lei YD, Teixeira C, Muir DCG and Bidleman TF (2005) 'Atmospheric distribution and long-range transport behavior of organochlorine pesticides in North America', *Environmental Science & Technology*, 39(2):409-420, doi:10.1021/es049489c

South Australia (Government of South Australia) (2015) *Environment Protection (Water Quality) Policy 2015*, South Australia, accessed May 2022.

SWA (Safe Work Australia) (n.d.) *Hazardous Chemical Information System*, SWA website, accessed May 2022.

Umegaki K, Ichikawa T (1988) 'Relationship between changes of drug metabolizing enzyme activities and toxicity following pentachlorobenzene administration in rats', *Eisei Kagaku,* 34:518-523, doi: 10.1248/jhs1956.34.518

Umegaki K, Ikegami S and Ichikawa T (1993) 'Effects of restricted feeding on the absorption, metabolism, and accumulation of pentachlorobenzene in rats'*, Journal of Nutritional Science and Vitaminology*, 39(4):11-22, doi:10.3177/jnsv.39.11

UNECE (United Nations Economic Commission for Europe) (2017) *Globally Harmonized System of Classification and Labelling of Chemicals (GHS) Seventh Revised Edition*, UNECE, accessed May 2022.

UNEP (United Nations Environment Programme) (2001) *The Stockholm Convention on Persistent Organic Pollutants (POPs)*, UNEP, accessed May 2022.

UNEP (United Nations Environment Programme) (2007a) *Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting. Addendum: Risk profile on pentachlorobenzene,* UNEP, accessed May 2022.

UNEP (United Nations Environment Programme) (2007b) *Other information provided by the intersessional working group on pentachlorobenzene*, UNEP, accessed May 2022.

US EPA (United States Environmental Protection Agency) (2017*) Estimation Programs Interface (EPI) SuiteTM for Microsoft® Windows, v 4.11.* [Computer Software], US EPA, accessed May 2022.

van Gestel CAM, Ma W-c and Els Smit C (1991) 'Development of QSARs in terrestrial ecotoxicology: Earthworm toxicity and soil sorption of chlorophenols, chlorobenzenes and dichloroaniline', *Science of The Total Environment*, 109-110:589-604, doi: 10.1016/0048-9697(91)90212-W

Vorkamp K, Riget F, Glasius M, Pécseli M, Lebeuf M and Muir D (2004) 'Chlorobenzenes, chlorinated pesticides, coplanar chlorobiphenyls and other organochlorine compounds in Greenland biota'*, Science of The Total Environment*, 331(1):157-175, doi: 10.1016/j.scitotenv.2004.03.027

Wang M-J and Jones KC (1994) 'Behaviour and fate of chlorobenzenes (CBs) introduced into soil-plant systems by sewage sludge application: A review', *Chemosphere*, 28(7):1325-1360, doi: 10.1016/0045-6535(94)90077-9

WHO-IPCS (WHO International Programme on Chemical Safety) (1991) *Environmental Health Criteria (EHC) 128: Chlorobenzenes other than Hexachlorobenzene,* WHO-IPCS, accessed May 2022.