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

Benzene, hexachloro- (HCB)

Evaluation statement

22 December 2022

Table of contents

Contents

AICIS evaluation statement

Subject of the evaluation

Benzene, hexachloro- (HCB)

Chemical in this evaluation

Name	CAS registry number
Benzene, hexachloro-	118-74-1

Reason for the evaluation

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

Parameters of evaluation

Hexachlorobenzene (HCB) is currently listed on the Australian Inventory of Industrial Chemicals (the Inventory). HCB was identified as a persistent organic pollutant (POP) at the first conference of parties to the Stockholm Convention on Persistent Organic Pollutants (the Stockholm Convention). The global use of HCB as industrial and agricultural chemical was prohibited under the Stockholm Convention in 2001. Australia has ratified the listing of HCB on the Stockholm Convention and implemented controls on the import, use and disposal of HCB.

This evaluation assesses the risks to workers, public and the environment from any potential introduction (by import and manufacture) 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 (HCB) is currently listed on the Inventory and may be introduced in Australia as a listed introduction under the *Industrial Chemicals Act, 2019 (IC Act).*

Data provided to the Office of Chemical Safety, which administers the Australian Industrial Chemicals Introduction Scheme (AICIS), indicates that the chemical is not manufactured or imported into Australia and the only introduction of the chemical is through unintentional production of HCB during manufacture of other chemicals. Chemicals incidentally introduced are considered excluded introductions under the *IC Act*.

The chemical was historically used as an intermediate in the manufacture of dyes and the synthesis of organic chemicals. At least 15 000 tonnes of HCB (as by product residues) were generated in Australia through industrial processes between 1963 to 1991 (Orica 2021).

Available evidence indicates that the chemical has non-industrial use as an agricultural fungicide; however, there is no specific information on volumes that were manufactured or imported historically (Barber et al. 2005).

Articles produced or imported containing HCB in the past are likely to remain in use and will be present in the environment for some time.

The chemical is still found in the environment because of past uses, emission from incomplete combustion and leachate from landfill (Nascimento et al. 2004).

Human health

Health hazard data considered relevant to the evaluation of the risks associated with exposure to HCB were primarily based on the information from the Agency for Toxic Substances and Disease Registry (ATSDR 2015), Government of Canada (1993) and International Agency for Research on Cancer (IARC 2001).

HCB is an organochloride that can cause systemic (liver, kidney, skin, bone, and thyroid), and neurological toxicity in animals and in humans. In animal studies, reproductive and developmental toxicity, and induction of cancer were reported following repeated exposure to HCB.

The chemical is expected to be readily absorbed following oral exposure from contaminated water, food, soil or breast milk through the digestive tract. HCB can also be absorbed through the lungs to a lesser extent (ATSDR 2015).

Summary of health hazards

HCB has low oral and inhalation acute toxicity in experimental animals. The reported oral median lethal dose (LD50) values were >10,000 mg/kg bw in rats and >1000 mg/kg bw in guinea pigs. The reported median lethal concentration (LC50) values were 1600 mg/m^3 in cats and 4000 mg/m^3 in mice (Government of Canada 1993; IARC 2001).

Based on the available data, the chemical is harmful following prolonged or repeated exposures. Adverse effects reported in various animal species following subchronic (<12 months) and chronic (≥12 months) oral exposures to HCB were mainly associated with the liver, kidneys, ovary, and central nervous system. Other effects reported include skin lesions (porphyria cutanea tarda); alteration in porphyrin metabolism (porphyria); behavioural changes; altered thyroid functions and serum levels of thyroid hormones; renal effects; and changes in calcium homeostasis and bone morphometry. Similar adverse effects were reported in a limited number of occupational studies where inhalation exposure to high concentrations of HCB in air was reported, and in subjects who ingested bread contaminated with HCB (ATSDR 2015; Government of Canada 1993).

The chemical was considered not to be genotoxic based on several in vitro and in vivo studies.

There is adequate evidence to suggest that HCB is carcinogenic to various experimental animals; however, there is insufficient evidence of the carcinogenic effects of HCB in humans. Increased incidence of tumour formation in the liver was reported in various animal studies following oral exposure to HCB. Other effects in various organs such as renal metaplasia, adenomas and renal cell carcinomas; lymphosarcomas; adrenal hyperplasia and

pheochromocytoma; parathyroid adenomas; and haemangioendothelioma; and thyroid tumours were also reported (ATSDR 2015; Government of Canada 1993; IARC 2001).

Incidences of thyroid cancer, soft tissue sarcoma and brain tumours were reported in male subjects exposed to HCB (average of 35 ng/m^3 HCB obtained from 40 ambient air samples) and residing near an organochlorine factory. The findings were isolated to males and based on a very small number of observed cases (Grimalt et al. 1994).

The IARC, the United States Environmental Protection Agency (USEPA) and the American Conference of Governmental Industrial Hygienists (ACGIH) concluded that HCB is an animal carcinogen and probably a human carcinogen (ACGIH 2014; IARC 2001; US EPA 2003).

Information available indicated reproductive and developmental toxicity in experimental animals following repeated exposure to HCB. Limited data are available concerning the reproductive and developmental toxicity of HCB in humans. Reported reproductive effects included increase testicular weight, testicular degeneration, and histopathological abnormalities of the ovaries (ATSDR 2015; Government of Canada 1993). An LOAEL of 0.01 mg/kg bw/day was determined based on the reported effects in the ovaries in a 90 day study in female Cynomolgus monkeys (ATSDR 2015).

Developmental effects including skeletal malformation, systemic and neurological effects, and foetal abnormalities were reported. Mothers exposed by eating HCB treated seed grain (containing approximately 10% HCB) passed HCB to their infants through the placenta and through breast milk (ATSDR 2015; Government of Canada 1993; IARC 2001).

Mothers diagnosed with porphyria were reported to have a high incidence of miscarriages and stillbirths and gave birth to children who died in the first several years of life (Gocmen et al. 1989).

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

Health hazards	Hazard category	Hazard statement
Specific Target Organ Toxicity (repeated exposure)	STOT Rep Exp. 1	H372: Causes damage to organs through prolonged or repeated exposure
Carcinogenicity	Carc 1B	H350: May cause cancer

Summary of health risk

Public

The chemical can cause cancer in experimental animals. Repeated long term exposure to HCB showed adverse effects on the liver, skin, bone, thyroid and CNS, exhibited reproductive and developmental toxicity, and caused occasional deaths in animals and in humans.

The public may be exposed to the chemical due to its introduction as an impurity in chemical products. However, given that the chemical is present at very low concentrations (≤0.0005%), this introduction is unlikely to pose a risk to the public.

There is a global phase out of manufacture and use of HCB; therefore, public exposure from use of articles containing HCB is expected to decline to minimal levels as the articles reach the end of their useful life. Public exposure as a result of past uses, emission from incomplete combustion and leachate from landfill is also expected to diminish.

Current controls in place to manage the risk to the environment include restrictions on import and subsequent use of the chemical. These existing controls should also manage the risk to the public from import and use of the chemical. However, there are no current controls in place to manage the manufacture of HCB in Australia. Whilst HCB is listed in the Inventory, it is authorised to be introduced as a listed introduction under the *Industrial Chemicals Act 2019 (IC Act)*. Australian manufacture of HCB could increase the risk to the public 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 public (see **Proposed means for managing risks**).

Workers

Workers may be exposed to the chemical due to its introduction as an impurity in chemical products. However, given the very low concentrations (0.0005%) this introduction is unlikely to pose a risk to workers.

Current controls in place to manage the risk to the environment include restrictions on import and subsequent use of the chemical; therefore, these existing controls should also manage any risk to workers. However, there are no current controls in place to manage the manufacture of HCB in Australia. Whilst HCB is listed in the Inventory, it is authorised to be introduced as a listed introduction under the *Industrial Chemicals Act 2019 (IC Act)*. Australian manufacture of HCB could increase the risk to 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

HCB is a Persistent Organic Pollutant (POP) as defined by the *Stockholm Convention on Persistent Organic Pollutants*. Therefore, this chemical has the characteristics of a POP as described in the criteria in Annex D to the Convention:

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

Environmental hazard classification

Classification of the environmental hazards under the GHS has not been conducted for this chemical.

Summary of environmental risk

The chemical is a POP 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 humans or animal life in the environment, and undergo long range transport to remote regions of the world. Since the chemical is a POP, there are significant long term risks to the environment from the manufacture and use of the chemical, including from introduction in articles. The inclusion of HCB in Annex A does not prevent the chemical being introduced as a manufacturing impurity.

No information on current industrial use of the chemical has been identified in Australia and it is not currently manufactured in Australia. The chemical is likely to be present as an impurity in a small number of chemical products. Based on available information, the risk to environment from its introduction as an impurity in chemical products is considered to be low.

Introductions authorised as a listed introduction

Since HCB is currently listed on the Inventory it may be introduced in Australia as a listed introduction under the *IC Act 2019.* Import of the chemical is prohibited under the *Customs (Prohibited Imports) Regulations 1956.* However, manufacture is not explicitly prohibited in Australia and, in principle, remains an authorised introduction whilst the chemical remains listed on the Inventory. This presents a potential risk to the environment that is not managed by existing risk management frameworks.

Advice on the existing risk management frameworks was sought from the Department of Climate Change, Energy, the Environment and Water (DCCEEW). DCCEEW advised that there are existing environmental risk frameworks in place to manage HCB, including listing under the *Customs (Prohibited Imports) Regulations 1956*. However, these frameworks cannot manage the environmental risks from the introduction of HCB (by manufacture).

Historical introductions and presence in articles

The chemical is likely to be present 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 HCB.

Proposed means for managing risks

Inventory listing

The Executive Director is not satisfied that the human health and environmental risks identified in this Evaluation Statement can be managed. Therefore, the Inventory listing for benzene, hexachloro- (HCB; CAS No 118-74-1) should be removed under Section 95 of the *Industrial Chemicals Act 2019*.

Environment

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

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 HCB and imported articles containing HCB.

Conclusions

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

HCB is a Persistent Organic Pollutant (POP) 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 Convention, Australia is bound by international law to prohibit and/or take legal and administrative measures necessary to eliminate the production and use of chemicals listed in Annex A.

Considering the human health and environmental effects of HCB 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 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 HCB 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.

HCB 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, HCB 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**).

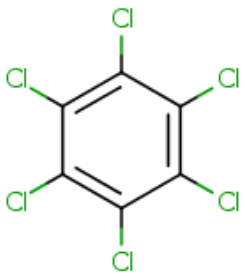
Supporting information

Rationale

HCB was identified as a persistent organic pollutant (POP) at the first conference of parties to the Stockholm Convention. Its global use as an industrial and agricultural chemical has been banned under this Convention since 2001. Australia has ratified and implemented controls on the import, use and disposal of HCB, predominantly on its use as a pesticide and the disposal of by-product residues generated from industrial solvent manufacture.

The previous National Industrial Chemicals Notification and Assessment Scheme (NICNAS) proposed to remove the chemical from the Inventory as a non-industrial chemical; however, public consultation at that time indicated potential ongoing use. This evaluation will assess the information provided from this consultation and review the regulatory status of the chemical under the *IC Act 2019*.

Chemical identity

Chemical Name	Benzene, hexachloro-
CAS RN	118-74-1
Synonyms	hexachlorobenzene HCB 1,2,3,4,5,6-hexachlorobenzene perchlorobenzene
Structural formula	
Molecular formula	C_6Cl_6
Molecular weight (g/mol)	284.8 g/mol
SMILES	C1(=C(C(=C(C(=C1Cl)Cl)Cl)Cl)Cl)Cl
Chemical description	Chlorinated aromatic compound

Relevant physical and chemical properties

Physical form	White crystalline solid with characteristic odour
Melting point	228 °C
Boiling point	325 °C
Vapour pressure	2.29 x 10^{-3} Pa at 25 °C
Water solubility	0.0062 mg/L at 25 °C
Henry's law constant	131 Pa·m^3/mol at 25 °C
Ionisable in the environment?	No
pKa	-
log K_{OW}	5.73

The chemical is a crystalline solid which is slightly soluble in water. The Henry's law constant of the chemical indicates a high volatility from aqueous media. The high logarithmic octanol-water partition coefficient (log K_{OW}) for this chemical indicates that it is highly lipophilic.

Introduction and use

Australia

Data provided to AICIS indicates that the only introduction of the chemical into Australia is through unintentional production during the manufacture of other chemicals. The chemical is identified as an impurity in products containing phthalocyanine pigments and isophorone diisocyanate, and may subsequently be present in:

- lubricants and greases
- adhesives
- surface coatings
- biological indicators.

The chemical is present at a maximum concentration of 0.0005% in these products.

Chemicals incidentally introduced during manufacture are considered excluded introductions under the *IC Act*. This introduction pathway is not considered an industrial use that requires compliance with the *IC Act*. Process and plant modifications to reduce unintentional production of this chemical are being implemented by industry, and current improvements in chemical manufacturing processes are expected to minimise the production of the incidentally produced chemical during manufacture in the future.

Historically, HCB was used as a chemical intermediate in the manufacture of dyes, rubber and synthesis of organic chemicals (solvents and chlorinated pesticides) (Barber et al. 2005).

Between 1963 and 1991, the manufacture of plastic and chlorinated solvents (carbon tetrachloride (CAS RN 56-23-5), perchloroethylene (CAS RN 127-18-4) and ethylene dichloride (CAS RN 107-06-2)) at Botany (NSW) produced 15 000 tonnes of HCB waste, which was stored in drums for eventual destruction (Orica 2021). In early 2017, 135 tonnes of this waste were exported and destroyed in Finland at an incineration facility, following an agreement between the Australian and Finnish governments in 2016. A further 1500 tonnes were approved for export in the same year after being repacked (Orica 2021). The remainder of the waste is in storage at Botany waiting for shipping and destruction.

The chemical had widespread use as a fungicide in Australia in the 1960s, when some 200 tonnes of technical HCB were used annually to treat wheat seeds (Barber et al. 2005). The chemical was banned in 1972 and there are no current APVMA registered products containing HCB as an active constituent (APVMA). Agricultural uses are not considered in this evaluation.

International

The chemical was first produced in North America in 1945. Global peak production was about 10 000 tonnes per year from 1978−1981, with 80% of the production in Europe (Barber et al. 2005).

The chemical was used mainly as a fungicide in most countries until the mid-1980s. Industrial uses included HCB as a raw material for synthetic rubber, as a rubber peptising agent in the manufacture of nitroso- and styrene type rubbers, as a plasticiser for PVC plastics, as a fluxing agent in the manufacture of aluminium, as a flame retardant and as a biocide in wood preservation. The chemical was also used as additive for pyrotechnic compositions for the US and Russian military as well as a porosity controller in manufacture of graphite anodes (Barber et al. 2005; NCBI).

The chemical is no longer used as an industrial chemical in other countries. However, the chemical may still be used in China and Russia as an intermediate in the production of the agricultural chemical, pentachlorophenol (CAS RN 87-86-5) (Barber et al. 2005; Kunisue et al. 2004).

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 hazard category and statements:

Health hazards	Hazard category	Hazard statement
Specific Target Organ Toxicity (repeated exposure)	STOT Rep Exp. 1	H372: Causes damage to organs through prolonged or repeated exposure
Carcinogenicity	Carc 1B	H350: May cause cancer

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

Environment

The chemical is listed in Schedule A of the proposed National Strategy for Management of Scheduled Wastes (ANZECC 1992). Although NSW is the only state that has prohibited the use and production of HCB (NSW EPA 2004), public awareness of its environmental risks led to the regulation of its movement and disposal under various state legislation (ACT 2000; *Environmental Protection Regulation 2019*; *Environment Protection (Water Quality) Policy 2015*).

The chemical is listed on Schedule 9 of the *Customs (Prohibited Imports) Regulations 1956*. Authorisation must be obtained from the responsible Minister before the chemical can be imported into Australia.

International regulatory status

United Nations

The chemical is listed as a persistent organic pollutant (POP) under the Annex A (elimination) and Annex C (unintentional production) of the Stockholm Convention (UNEP 2001). The listing prohibits production and use of the chemical. Member countries must make an effort to reduce the unintentional production of this chemical that may occur in the manufacture of other chemical products. Australia has ratified and implemented controls on HCB following listing in the Annexes of the Stockholm Convention.

HCB is also listed on the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade (UNEP and FAO 1998).

Canada

Use of HCB was withdrawn in 1976 and banned in 2003 (Government of Canada 2017). The chemical is listed under and subject to the Prohibition of Certain Toxic Substances Regulations, 2012, which prohibits the manufacture, use, sale, offer for sale or import of certain toxic substances, and products containing them, with a limited number of exemptions.

The chemical was also listed under the *National Pollutant Release Inventory in 2016* (Government of Canada 2017).

European Union

The use of HCB is prohibited under *Commission Regulation No 850/2004 on Persistent Organic Pollutants (EC 2004)*. HCB is listed in: *Annex I - List of substances subject to*

prohibitions; Annex III - List of substances subject to release reduction provisions; and *Annex IV - List of substances subject to waste management provisions.*

The chemical is now subject to the ECHA substance regulatory obligations for being carcinogenic and a POP listed under Annex A and C of the Stockholm Convention (ECHA).

New Zealand

The chemical was banned in 2004 (Ministry for the Environment 2018), and it is not listed in the New Zealand Inventory of Chemicals (NZIoC).

United States of America

Use of HCB was restricted in 1984. The chemical is listed under the EPA Toxic Release Inventory (US EPA 2021).

Asia

The chemical was banned in Japan in 1979. HCB is listed under Class I, as a substance that is persistent and highly bioaccumulative (NITE 1975). HCB was never registered as an agricultural product in Japan, but was produced as a raw material for the manufacture of pentachlorophenol and other chlorinated chemicals (Barber et al. 2005).

Health hazard information

Toxicokinetics

In animals and in humans, absorption of ingested HCB from the digestive tract is likely to include circulatory mechanisms, where tissue distribution is preferentially to fat tissues due to its lipophilic nature, and via passive diffusion. Levels of HCB in blood have been reported to be lower in lactating mothers (in animals and in humans) because of its lipophilicity (ATSDR 2015).

The chemical is slowly metabolised by hepatic cytochrome P-450 enzymes by conjugation with glutathione, glucuronide and sulfate, and by reductive dichlorination; and converted to pentachlorophenol (PCP) (ATSDR 2015).

In rats, HCB is excreted in the urine mainly as tetrachlorohydroquinone, pentachlorobenzene, pentachlorophenol, pentachlorothiophenol, and pentachlorothioanisole. HCB is eliminated in the faeces predominantly as unchanged parent compound (ATSDR 2015).

In humans, HCB accumulates in fat tissues. It is reported that pregnant mothers transfer HCB from the blood across the placenta to their unborn child; and in nursing mothers, transfer is to the breast milk; hence, breast fed babies from mothers exposed to HCB may have higher levels of HCB. HCB was found in human milk samples from the general population at concentrations between 11-70 ng/g fat (ATSDR 2015).

Acute toxicity

The chemical has low acute toxicity with reported oral LD50 of 3500 to >10 000 mg/kg bw in rats and >1000 mg/kg bw in guinea pigs. No effects were found following a single inhalation

exposure (4 hours) of 4.4 mg/m^3 in Sprague Dawley (SD) rats (Government of Canada 1993). An LC50 value for inhalation exposure of 1600 mg/m^3 was reported for cats (IARC 2001).

Repeat dose toxicity

Animal studies

In several short term, repeated (sub-chronic <12 months) and long term repeated (chronic >12 months) studies in rats, oral exposure to HCB caused liver effects including porphyria and other hepatic changes such as peribiliary lymphocytosis, fibrosis, hepatomegaly, increased liver weight, increased hepatic enzyme levels and degenerative pathological changes. A no observed adverse effect level (NOAEL) of 4 mg/kg bw/day was determined for female rats following 4 months dietary exposure to HCB based on increased levels of liver porphyrins and α-aminolevulinic synthase. Disturbance of the haem biosynthesis pathway of porphyrin metabolism in the liver (porphyria), resulted in abnormal levels of porphyrin precursors in rodents following long term exposure to HCB.

Some evidence of kidney damage was reported in various animals. Various dose feeding studies in rats between 12–16 weeks identified lowest observed adverse effect level (LOAEL) values between 19–56.5 mg/kg bw/day, and NOAEL values between 5–11.3 mg/kg bw/day for increased kidney weight in both sexes (ATSDR 2015). LOAEL and NOAEL of 5 and 0.5 mg/kg bw/day, respectively were reported in pigs orally treated with HCB for 90 days, based on increased kidney weights (Den Tonkelaar et al. 1978).

An NOAEL of 0.1 mg/kg bw/day based on bone related abnormalities was reported in rats orally dosed with HCB for up to 15 weeks (ATSDR 2015; Government of Canada 1993). Increased thyroid weight, decrease in total thyroxine (T4) levels, and increased thyroid stimulating hormone level (TSH) were reported in animals orally exposed to high levels of HCB (Den Tonkelaar et al. 1978). Histopathological observations including large and irregularly shaped follicles in the thyroid were reported in hamsters fed with 47.4 mg/kg bw/day HCB for 6 weeks, or 19.0 mg/kg/day HCB for 18 weeks or 28 weeks (Smith et al. 1987).

Observation in humans

A number of occupational studies have associated long term repeated exposure to HCB with liver effects (increased porphyrins), skin lesions and neurological effects.

Studies of workers from an organochlorobenzene factory (n=185) and nearby residents (n=604) of Flix, Spain found an association between exposure to high environmental levels of HCB (35 ng/m^3 as a 24-hour average in air), and elevated HCB blood levels and hepatic effects (increased hepatic enzymes) (Sala et al. 2001).

In a separate study conducted in 241 residents (Sunyer et al. 2002), elevated levels of urinary porphyrin were reported. In 68 neonates who provided urine samples on the third day of life, 52 were followed up until the age of 4. Urine samples collected from these children had increased levels of total porphyrins and coproporphyrins with increasing levels of HCB. The increase in urinary coproporphyrins suggested an early onset of toxic effect on the hepatic haem pathway (Sunyer et al. 2008). High concentrations of HCB were found in foetal cord blood and maternal serum (ATSDR 2015).

Blood samples collected from residents (n=608) and workers (n=189) showed a

non-statistically significant increase in levels of serum creatinine in the presence of high levels of HCB in blood. The NOAEL for liver effects in the Flix residents' study was reported to be 0.000035 mg/m^3 for 40 years of occupational exposure to HCB (ATSDR 2015).

Epidemiological studies were conducted in a population exposed to HCB by ingestion of bread made from grain treated with HCB (10%) as a pesticide in the 1950's in Turkey. The ingested dose of HCB was estimated to be in the range of 0.05–0.2 g/day, equivalent to 0.7–2.9 mg/kg/day for an average 70 kg person. A very high mortality rate occurred in infants under the age of 2 years who had been breast fed by mothers who ingested the contaminated bread. Infants displayed skin lesions (blistering and annular erythema), a condition known as pembe yara or "pink sore". Infant deaths were primarily linked with cardiorespiratory failure, secondary to the skin lesions. Other clinical symptoms reported include weakness and convulsions prior to death. A disease called kara yara or "black sore" was observed mostly in children between the ages of 6 and 15 years, although younger children and adults were also affected. The skin condition appeared after approximately 6 months of exposure. Symptoms included photosensitivity, skin fragility (causing ulcers and scarring), hyperpigmentation, and hirsutism (growth of hair in unusual amounts and locations). These skin lesions were identified as porphyria cutanea tarda, a type of porphyria or blood disorder that affects the skin. Other symptoms reported were neurological symptoms such as loss of appetite, weakness, arthritis (swelling and spindling of the fingers, but with little pain); hepatomegaly; enlarged thyroid; and effects on locomotor skills (Cripps et al. 1984; Peters et al. 1982; Peters et al, 1987).

Follow up studies at 25 (Peters et al. 1982) and 30 years (Cripps et al. 1984) included 161 and 204 patients, respectively. The studies found neurological symptoms persisted in adults who had been exposed as children. Symptoms included weakness, paresthesia (spontaneous tingling or burning sensations), sensory shading (graded sensory loss that diminishes upon testing more proximally and indicative of polyneuropathy), myotonia (delayed muscle relaxation after an initial contraction), and cogwheeling (irregular jerkiness of movement due to increased muscle tone as seen in Parkinson's disease).

Genotoxicity

The chemical gave equivocal results in bacterial reverse mutation assays in *Salmonella typhimurium* and *Escherichia coli* with and without metabolic activation, although an assay for reverse mutation in the yeast *Saccharomyces cerevisiae* was reported as positive (ATSDR 2015; Government of Canada 1993; IARC 2001).

Reports indicated that the chemical did not produce chromosomal aberrations in human peripheral lymphocytes in vitro (ATSDR 2015; Government of Canada 1993; IARC 2001) but produced weak positive results in assays for DNA fragmentation and micronuclei formation in human hepatocytes (ATSDR 2015; IARC 2001).

Negative results were observed in 2 dominant lethal mutation assays in rats treated orally at doses ranging from 60 to 221 mg/kg (ATSDR 2015; Government of Canada 1993; IARC 2001). No evidence of genotoxicity was observed in mouse liver, lung, kidney, spleen, or bone marrow after oral dosing (ATSDR 2015).

Carcinogenicity

Animal studies

In several animal studies (rats, mice, hamsters), increased incidence of tumour formation in the liver was reported following exposure to HCB.

A statistically significant increase in the incidence of liver cell tumours (hepatomas) was reported in male and female Syrian golden hamsters fed diets containing 50, 100 or 200 parts per million (ppm) HCB (equivalent to 4, 8 and 16 mg/kg bw/day) for life. At 200 ppm, reduced survival in both sexes, and reduced weight gain and increased incidence of alveolar adenomas of the lung in males were reported. Significant increases in the incidence of haemangioendotheliomas of the liver were reported in both sexes at 200 ppm and in males at 100 ppm (Cabral et al. 1977; Cabral and Shubik 1986).

Swiss mice (both sexes) were fed a diet containing 0, 50, 100 and 200 ppm HCB (0, 6, 12 and 24 mg/kg bw/day) for 120 weeks. At 90 weeks, 4% of males survived, and all females died. Reduced body weight was reported at 50 and 200 ppm in females, and at 100 and 200 ppm in males. At 100 and 200 ppm, increases in the incidence of liver cell tumours (hepatomas) were reported for both sexes, but this was only significantly increased in females at 200 ppm. In both sexes, the tumour incidence was dose related not only in the number of animals with tumours but also in the latency period, and in the occurrence and size of tumours (Cabral et al. 1979; Cabral and Shubik 1986).

Weanling SD rats were fed diets containing 0, 0.32, 1.6, 8 or 40 ppm HCB (equivalent to 0, 0.01, 0.05, 0.27 and 1.39 mg/kg bw/day in males and 0, 0.01, 0.07, 0.35 and 1.72 mg/kg bw/day in females). After 3 months, F0 rats were bred and F1 pups (50 pups/sex) were selected from each dose group. From weaning, F1 pups were continued on the same diet for their lifetimes (up to 130 weeks). Increased incidences of neoplastic liver nodules and adrenal phaeochromocytomas were reported in F1 females exposed at the highest dose. A significantly increased incidence of parathyroid adenomas was reported in males at 40 ppm (Arnold et al. 1985).

In another study, weanling SD rats were fed diets containing 0, 75 or 150 ppm HCB (4 and 8 mg/kg bw/day for males and 5 and 9 mg/kg bw/day for females) for up to 2 years. Statistically significant increases in the incidence of hepatomas or hemangiomas and renal cell adenomas were reported at both doses in both sexes that survived after 1 year of treatment. Increased incidences of hepatocellular carcinomas and bile duct adenomas/carcinomas were also reported in females at both doses (ATSDR 2015; Government of Canada 1993; IARC 2001).

The chemical was administered by gavage (in corn oil with 1% acetone) to female SD rats (10/group) once per day, 5 days/week at doses 0, 0.03, 0.1, 0.3, 1.0, 3.0, 10, and 25 mg/kg bw/day for 90 days. Significant increases in incidences of mammary gland hyperplasia at the highest dose tested were reported (NTP 2002).

The National Toxicology Program (NTP) concluded that HCB is reasonably anticipated to be a human carcinogen (NTP 2014). US EPA classified HCB based on weight of evidence as Group B2 (Probably Carcinogenic to Humans) (US EPA 2003).

Observation in humans

The incidences of thyroid cancer, soft tissue sarcoma and brain tumours were increased between 1980-1989, in male subjects exposed to HCB and residing near the organochlorine factory. In 1989-1992, an average of 35 ng/m^3 HCB was obtained from 40 ambient air samples (Grimalt et al. 1994). The tumour incidences were not seen in females and the findings in males were based on a very small number of observed cases (2-3 for the various tumour types). Therefore, the evidence of cancer effects of HCB is limited and regarded as inconclusive in this study. In another case study, a 65 year old male believed to have been

exposed to airborne HCB and other organochlorine compounds at an aluminium smelter from 1967 to 1973 was diagnosed with hepatocellular carcinoma in 1985 (ATSDR 2015).

The association of porphyria and subsequent development of liver cancer was investigated in subjects exposed to HCB. However, other factors such as liver pathology and age were found to be better predictors in the subsequent development of tumours than levels of porphyrin found in these studies (ATSDR 2015).

Reproductive toxicity

Animal studies

In a multigenerational study, male and female SD rats received HCB in the diet at doses ranging from approximately 0.9 to 63 mg/kg bw/day through premating and 2 series of mating, gestation, and lactation for up to 4 generations. Statistically significant decreases in fertility and increases in the number of stillbirths were observed at approximately 28 mg/kg bw/day (parental males) and 31 mg/kg bw/day (parental females). At doses of ≥14 mg/kg bw/day (parental males) and ≥16 mg/kg bw/day (parental females), the average litter size was decreased (ATSDR 2015; Government of Canada 1993). No reproductive toxicity was observed in 2 successive litters from female SD rats receiving HCB in the diet (ATSDR 2015; Government of Canada 1993; IARC 2001). No reproductive effects were observed in a study where both male and female SD rats received HCB in the diet at estimated doses up to 3.4 mg/kg bw/day (males) and 3.9 mg/kg bw/day (females) from 3 months prior to mating through to weaning of the F1 offspring (Arnold et al. 1985).

In male Fischer 344/N rats dosed orally with HCB in arachis oil at approximately 16 mg/kg bw/day for 90 weeks, testicular weight was significantly increased compared with controls (ATSDR 2015; Government of Canada 1993).

Female beagle dogs administered gelatin capsules containing HCB in corn oil at doses up to 100 mg/kg bw/day for 21 days showed no histopathological abnormalities of the ovaries (ATSDR 2015). Slight testicular degeneration, with numerous spermatogenic giant cells and incomplete complement of spermatogonia in the seminiferous tubules, was observed in 2/6 male beagle dogs dosed at 110 mg/kg bw/day gelatin capsules containing HCB in corn oil for 12 months (ATSDR 2015; Government of Canada 1993).

Retarded sexual maturation of the testes was observed in male SPF pigs fed 50 mg/kg bw/day of HCB for 90 days. No effects were reported at lower doses of up to 5 mg/kg bw/day (Den Tonkelaar et al. 1978).

Oral administration of 0.01 mg/kg bw/day (lowest dose tested) for 90 days caused ovarian lesions in adult female Cynomolgus monkeys (ATSDR 2015). Ultrastructural analyses of developing ova showed mitochondrial changes, which increased in frequency and severity with dose. Swelling of the cristae resulting in abnormal intracristae spaces was seen at 0.01 mg/kg bw/day; mitochondrial matrices were coarsely granular and exhibited occasional irregular morphology at 0.1 mg/kg bw/day; and mitochondria had “electron lucent” matrices and reduced membrane integrity at 10 mg/kg bw/day. Increased frequency and severity of lesions in follicular cells (abnormal nuclei) were observed at 0.01 mg/kg bw/day, while nuclear membrane infolding was clearly apparent at 0.1 mg/kg bw/day. A LOAEL of 0.01 mg/kg bw/day was determined from this study. In another 90 day study, female Cynomolgus monkeys had dose related degenerative changes in oocytes and ovaries at all doses tested (0.1–10 mg/kg bw/day) (ATSDR 2015; Government of Canada 1993).

In female Rhesus monkeys dosed with HCB for 60 days, ovarian effects were reported at 8 mg/kg bw/day. The ovarian effects included cortical degeneration, reduced numbers of primary follicles with a concurrent increase in relative corpora lutea volume, multiple follicular cysts, and thickening of the ovarian germinal epithelium with cells exhibiting a columnar appearance progressing to pseudostratification. These effects increased in incidence and severity with dose. Results from a lower dose study indicated no changes in serum levels of oestrogen, progesterone, FSH, or LH in female Rhesus monkeys fed 0.03 mg/kg bw/day HCB in monkey chow for 11 months (ATSDR 2015).

Observation in humans

In a follow up study conducted between 1977 and 1981 of the Turkey epidemic, 42 porphyric mothers were reported to have been exposed as children, with 188 pregnancies (Peters et al. 1982, 1987). These mothers were reported to have high incidence of miscarriages and stillbirths and produced children who died in the first several years of life (Gocmen et al. 1989). Similar effects were reported in another follow up study (57 porphyric mothers, who had a total of 276 pregnancies) conducted 20–30 years after initial exposure. Porphyric mothers had an average of 0.51 ppm hexachlorobenzene in their breast milk, compared to 0.07 ppm in unexposed controls (Gocmen et al. 1989).

A subsequent retrospective study was conducted 40 years after initial exposure to compare 3 groups of 42 women (controls from outside the exposed region and women from the HCB exposed region either with or without a diagnosis of porphyria cutanea tarda) (ATSDR 2015; IARC 2001). The incidence of women with blood levels of HCB exceeding 1 ng/mL was greater in women with porphyria cutanea tarda or women from an HCB exposed region than controls living outside the exposed region and correlated (across exposure groups) with increased risk of spontaneous abortion. Statistically significant increases in the levels of inhibin (a hormone secreted by ovarian granulosa cells to decrease the release of FSH from the pituitary) were reported to be observed in women diagnosed with porphyria cutanea tarda.

No significant associations were reported between serum HCB and serum testosterone levels among 257 adult male and 436 adult female Native Americans (Mohawks) or among 341 adult men from a fertility clinic (ATSDR 2015). In a cross-sectional study, no significant associations were found between 304 men and 300 women from a rural area of Brazil heavily contaminated with organochlorine pesticides, and serum HCB and serum testosterone levels in men or serum estradiol, progesterone, prolactin, luteinizing hormone (LH), or FSH in premenopausal women (ATSDR 2015).

In Spain, females (n=46–60) exposed to HCB while working at an electrochemical factory suffered spontaneous abortions and had given birth to infants with low birth weight, and congenital malformations (Sala et al. 1999b). Based on 63 cases, a statistically significant association between prenatal exposure to HCB and impaired development of locomotor skills in newborns from mothers working at the factory compared with those living in the nearby villages was reported (Sala et al. 1999a).

Developmental toxicity

Animal studies

In a 15 day developmental toxicity study in pregnant Wistar rats orally treated with HCB, increased incidences of sternal variations and 14th rib formation were reported at ≥40 mg/kg bw/day. Decreased foetal and maternal body weights were seen with other maternal effects at ≥80 mg/kg bw/day (ATSDR 2015; Government of Canada 1993).

Female SD rats were gavaged for 4 days with 2.5 or 25 mg/kg bw/day of HCB, 2 weeks prior to mating. Pups from both treatment groups reoriented themselves in a negative geotaxis test, required less time in an olfactory discrimination test (postnatal days 6, 8, and 10), and demonstrated increased exploratory activity in a motor activity test (postnatal days 15–20). Pups exposed to 25 mg/kg bw/day exhibited decreased acoustic startle response (ASR) on postnatal day 23 and increased ASR on postnatal day 90. A LOAEL of 2.5 mg/kg/day was determined from this study (ATSDR 2015; IARC 2001).

Male and female SD rats were fed HCB 3 months prior to mating through to weaning. Pups were continued on the same diet for their lifetimes. The high dose group (estimated doses of 2.8 and 3.2 mg/kg bw/day for F0 parental males and females, respectively) exhibited decreased pup survival. When examined as adults (week 130), treatment related effects in F1 males included peribiliary lymphocytosis and fibrosis at 0.022 mg/kg bw/day and hepatic basophilic chromogenesis at ≥0.55 mg/kg bw/day. An LOAEL of 0.022 mg/kg/day was determined from the study (Arnold et al. 1985).

Pups of pregnant BALB/c mice fed doses as low as 0.5 mg/kg bw/day HCB on gestation days 1–18 exhibited significant decrease in delayed type hypersensitivity (DTH) response when tested on postnatal day 45 (ATSDR 2015; Government of Canada 1993; IARC 2001).

A single dose study found an increase in the overall incidence of foetal abnormalities including cleft palate and renal agenesis in the foetuses of pregnant female CD-1 mice gavaged with 100 mg/kg bw/day of HCB on gestation days 7–16 (ATSDR 2015; Government of Canada 1993).

Only one of 3 infant rhesus monkeys (between 21 and 118 days of age) nursing from mothers fed 64 mg/kg bw/day HCB by daily gavage survived (the durations of dosing were 15 and 38 days (for the mortalities) and 60 days (for the survivor)). No maternal effects were reported. Infants exhibited neurological effects (listlessness, lethargy, depression, and ataxia) and lung oedema prior to death. Microscopic findings included mild hepatocellular hypertrophy in the infant that survived, and hepatic fatty changes, slight renal proximal tubule vacuolation, and mild cerebral gliosis in one or both infants that died (ATSDR 2015; IARC 2001).

Observation in humans

In Spain, females (n=46–60) exposed to HCB while working at an electrochemical factory suffered spontaneous abortions and had given birth to infants with low birth weight, and congenital malformations (Sala et al, 1999b). Based on 63 cases, a statistically significant association between prenatal exposure to HCB and impaired development of locomotor skills in newborn from mothers working at the factory compared with those living in the nearby villages was found (Sala et al. 1999a).

Changes in anthropometric measurements including prematurity, shorter length of gestation and crown heel length were observed in 70 infants from mothers living near the factory. Cord serum levels of >1.48 ng/mL HCB were found to be associated with smaller crown heel length and shorter length of gestation (ATSDR 2015). The study was limited by small sample size.

An epidemiological study in Australia reported HCB concentrations ranging from trace amounts to 8.2 ppm in human body fat and ≤0.41 ppb in whole blood. No adverse health effects or mortality associated with these levels were reported (ATSDR 2015).

In a case control study in Rome, Italy, 80 hypospadia cases and 80 controls from 2 hospitals reported significantly ($p<0.05$) increased risk of hypospadias with each increase of 10 pg/g HCB in the maternal serum. In Sweden, another case control study of 237 hypospadia cases and 237 controls, showed increased risk of hypospadias among mothers with serum HCB levels >0.26 ng/mL compared with those mothers with lower serum HCB levels (ATSDR 2015).

Environmental exposure

The chemical has no industrial uses in Australia but is present as an impurity in some industrial products. Current releases of HCB from industrial products are expected to be negligible compared to releases from other sources.

Information provided to AICIS indicates HCB is present as an impurity in some specialty chemical products. HCB is present as an impurity at a low concentration in phthalocyanine pigments and bulk supplies of isophoronediisocyanate, a monomer used in the preparation of adhesives and hard setting enamel paint products. Pigments and bulk isophoronediisocyanate will be blended into chemical products such as adhesives, greases, and coatings. The reported concentrations of HCB in these products are up to 5 ppm or up to 5 grams of HCB per tonne of product. Available information indicates that these products are predominately used in a commercial setting and are not widely available to the public.

Adhesive and coating products will be applied to a substrate; however, the HCB in these products is expected to be contained within the cured product matrix. HCB may migrate out of the finished product over its lifetime; however, the bulk of the chemical is expected to share the fate of the substrate to which it has been applied and is; therefore, predominantly expected to be disposed of to landfill. Similarly, greases are commonly used in sealed-for-life components that are not expected to leak or require “topping up”. Therefore, the release of HCB is only likely to occur during disposal of greased products.

Exposure to the environment through use of these products is likely to occur only in landfills and expected to be minimal due to the very low volumes of HCB expected to be present.

Emissions of HCB to the environment are known to occur from several non-industrial sources (Barber et al. 2005). Although HCB is no longer used as an agricultural or industrial chemical, emissions occur from:

- direct emissions to air from the incomplete combustion of solid organic wastes in open landfills and municipal incinerators
- landfill leachates of waste materials from the manufacture of chlorinated solvents and chlorinated pesticides
- diffuse emissions from agricultural fields that result from either former application of HCB as a fungicide or impurities present in currently used chlorinated pesticides (for example, chlorothalonil, quintozene).

The amount of HCB released into the environment worldwide in the mid 1990s was estimated at 10–90 tonnes/year, of which 0.56–56 tonnes/year originated from municipal solid waste incineration (Bailey 2001). The European Union and the United States of America account for 45% of the global emissions (Barber et al. 2005).

Deliberate industrial use and manufacture of HCB could considerably increase the volumes of HCB released to the environment through industrial pathways.

Environmental fate

Partitioning

The chemical partitions to soil after release to the environment.

HCB is a slightly volatile and lipophilic neutral organic chemical that is very slightly soluble in water. Any HCB present in the atmosphere is found almost exclusively in the gas phase, with less than 5% associated with particles in all seasons except winter, where levels are still less than 10% particle-bound (Cortes et al. 1998).

HCB volatilises from water under normal atmospheric conditions, as indicated by a high Henry's Law constant of 131 $Pa \cdot m^3/mol$. In soil, HCB is expected to be largely immobile, as predicted by log Koc = 4.31 (Barber et al. 2005). However, the presence of HCB in leachates from landfill provides clear evidence that the chemical migrates through the soil horizons in the direction of water flow. The dispersal of HCB in leachates is likely due to transport with dissolved organic matter in the water moving through the soil profile (Nascimento et al. 2004).

Calculations with a standard multimedia partitioning (fugacity) model assuming equal and continuous emission of HCB to the air, water and soil compartments (Level III approach) predict that the majority of the chemical will partition to soil (84.1%) and sediment (12.6%) with minor amounts partitioning to air (1.1%) and water (2.2%) (US EPA 2017).

Degradation

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

HCB may be slowly degraded in the atmosphere by photolysis or by chemical reaction with hydroxyl radicals. Half lives in air have been estimated between 230 and 2292 days for tropical and polar regions, respectively (Brubaker and Hites 1998; Wania and Mackay 1995).

HCB may be slowly removed from water by photolysis, with a half life of about 70 days. In surface waters, hydrolysis is not a major route of dissipation as HCB tends to partition to sediment and particulate matter in this compartment. Suggested half lives range from 2.7 to 5.7 years in surface water and 5.3 to 11.4 years in groundwater based on the absence of biodegradation (Barber et al. 2005). Only one anaerobic bacterial strain is known to degrade, chlorobenzenes (Adrian and Görisch 2002).

The persistence of HCB in soil is mediated by its strong adsorption to organic matter which makes it largely unavailable to microorganisms. Soil dissipation half lives are estimated between 260 and 7300 days (20 years), but these losses are mostly by volatilisation rather than biodegradation. A half life of 11.7 years for sewage-sludge treated soils has been reported (Barber et al. 2005; UNEP 2007). Methanogenic bacteria, sulfate reducing and nitrate reducing microorganisms can dechlorinate HCB under these conditions leading to the production of pentachlorobenzene (PeCB, CAS RN 608-93-5) and less toxic chlorinated benzenes as the only metabolites (Brahushi et al. 2004).

Degradation in plants has been reported at loss rates between 0.1 and 0.8% per week. Aquatic organisms such as mussels and fish slowly metabolise HCB after uptake (Barber et al. 2005). The main metabolism pathway of HCB in mammals involves oxidation by P450 enzymes to produce phenolic compounds and reductive dechlorination to produce lower

chlorinated benzenes. A small proportion is conjugated and eliminated in faeces and urine (Renner 1988).

Bioaccumulation

The chemical bioaccumulates in tissues of organisms. The chemical has demonstrated biomagnification through food chains because it is not easily metabolised.

Accumulation of HCB in vegetation through wet or dry atmospheric deposition results in its incorporation into terrestrial food chains. Bioconcentration of HCB in the aquatic environment is the result of both direct uptake from water, and from food chain transfers. Mussels, oysters and fish show higher HCB concentrations in regions where high emissions of this chemical occur. In one study, average and highest levels of HCB in Australian fish were 4.2 and 60 ng/g wet weight (ww), respectively (Kannan et al. 1995). In another study, pelagic fish caught off the coast of Sydney had levels of HCB in the range of 116–871 ng/g ww (Mortimer and Connell 1995).

Bioconcentration factors (BCFs) of 3000 to >35 000 have been reported, along with evidence for biomagnification along food chains (IPCS 1997). Significant bioaccumulation of HCB in krill, mussels, oysters, fish, marine birds and mammals has been observed, with biomagnification factors (BMF) in seals (7.3) and marine birds (9.3–36.6) being an order of magnitude higher than in fish (Hop et al. 2002).

HCB accumulates in the blood, liver, kidney, brain and fat tissues of animals, and is also found in their faeces (Wang et al. 2020). Reptiles and birds also accumulate HCB in their eggs (Becker et al. 2001). Major metabolites found in animals are pentachlorophenol (CAS RN 87-86-5) and pentachlorobenzene, which are POP chemicals, while smaller amounts are degraded to lower chlorinated benzene and phenolic compounds (Renner 1981).

Environmental transport

Atmospheric long range transport of HCB has been demonstrated both by worldwide monitoring and modelling.

Historically, higher atmospheric concentrations were found near solvent and plastic manufacturing plants than in agricultural areas. HCB has been detected in areas far from the sources: in the High Tatras and Pyrenees mountains of Europe (van Drooge et al. 2004), in the Arctic (>100 pg/m^3), the Antarctic (60 pg/m^3) and the Southern Ocean (Bidleman et al. 1993). Recent monitoring data show steady concentrations of HCB at 74-84 pg/m^3 around the Great Lakes region of North America (Cortes and Hites 2000) and 23-70 pg/m^3 in the Lake Taihu region of China (Qiu et al. 2004). Higher levels in summer than in winter suggest strong volatilisation from the soil sources (Barber et al. 2005).

Past soil inputs of HCB persist due to the long half lives of the chemical in this medium, but worldwide levels in soil have decreased since its peak in the late 1980s. Typical soil concentrations range from 0.01 to 5.2 ng/g dry weight (dw) and correlate positively with the amount of soil organic matter (Barber et al. 2005). Due to its immobility, soil concentrations of HCB tend to reflect the baseline contamination of a region, and average values of >0.2 ng/g dw have been reported for Australia (Cavanagh et al. 1999). However, dust deposition contributes to soil contamination in remote mountainous areas (Ribes et al. 2002). The highest levels of HCB in soil are found in landfill areas of Brazil and industrial dumps of Europe, with concentrations in the range 337–6480 ng/g dw (Barber et al. 2005).

Significant amounts of HCB have been found in fresh waters of the world as a result of effluent inputs from HCB production plants and other industries, and run-off from agricultural fields. Water concentrations in Brazilian rivers (6–14 µg/L) are orders of magnitude higher than peak levels (75–100 ng/L) reported in industrial catchments of Europe and North America (Barber et al. 2005). Recent monitoring data show average concentrations of 12–140 pg/L in the USA (Petty et al. 2004) and 0.5–20 pg/L in remote regions of New Zealand and Ecuador (Barber et al. 2005). Levels of HCB in estuaries and coastal waters tend to be lower than in rivers due to the increased sedimentation and volatilisation rates that remove it from the water column.

Due to its low water solubility and persistence, HCB frequently accumulates in the sediment compartment. HCB concentrations in source regions of the world average about 1 ng/g dw. A residence time between 1.5 and 135 years was estimated for HCB in the Mediterranean coastal water column (Barber et al. 2005). The highest average levels of HCB in river sediments (6000 ng/g dw) are found in cities of Brazil (Del Grande et al. 2003), while the highest levels in marine sediments (871 ng/g) were found offshore from the Malabar outfall in Sydney, which contains a large proportion of industrial waste (Mortimer and Connell 1995).

Predicted environmental concentration (PEC)

No PEC is estimated, given that HCB is no longer used in Australia and any releases to the environment from previous uses cannot be determined — see the Environmental transport section for global environmental monitoring information.

Environmental effects

The chemical has been found in organisms across many environmental compartments and trophic levels and is highly bioaccumulative. This indicates a concern for chronic effects to predators and other high trophic level organisms that consume contaminated prey. Exposure to some mammalian predators and birds through diet indicate potential adverse reproductive effects at low to medium concentrations. The chemical also exhibits toxic effects to the reproduction of aquatic organisms over long term exposure timeframes.

HCB undergoes slow degradation in the environment to form other toxic chlorinated chemicals, such as pentachlorophenol and pentachlorobenzene.

Effects on Aquatic Life

The chemical shows toxic effects in aquatic organisms over long term exposure timeframes. The chemical does not appear to be acutely toxic to model organisms in studies testing for standard adverse effects such as mortality and immobilisation; however, HCB has shown acute toxic effects in tests using non-standard endpoints such as DNA expression in algae.

HCB has a very low water solubility and high volatility from water; a combination of properties that makes aquatic toxicity testing of the chemical very difficult. Many available studies in the literature report effect endpoints greater than the water solubility of HCB. This evaluation only considers studies that include endpoints below the solubility limit, or studies with endpoints higher than the solubility limit, where observed adverse effects could be verified.

Acute toxicity

The following measured median effective concentration (EC_{50}) value for algae was retrieved from the scientific literature (Figueroa and Simmons 1991):

Taxon	Endpoint	Method
Algae	48 h EC50 = 0.002 mg/L	*Cyclotella meneghiniana* (diatom) DNA reduction

All available acute toxicity data obtained following standard OECD methodology gave endpoints greater than the solubility limit of HCB. For many of these tests no adverse effects were observed on test organisms. Absence of adverse effects may be due to a lack of acute toxicity or due to lower than expected effective concentrations as a result of the partitioning behaviour of the chemical.

A non-standard toxicity test measuring DNA expression in algae indicates that toxic effects can occur after acute exposure to concentrations of HCB at and below its solubility limit.

Chronic toxicity

The following lowest observed effective concentrations (LOEC) and the 10th percentile effective concentration (EC10) value for aquatic organisms across 2 trophic levels were retrieved from the scientific literature (Calamari et al. 1983; Scheubel 1984):

Taxon	Endpoint	Method
Invertebrates	14 d LOEC = 0.023 mg/L*	*Daphnia magna* (water flea) 80% reduction in reproduction semi static
	21 d EC10 = 0.0009 mg/L	*Daphnia magna* (water flea) reproduction Semi static
Algae	96 h LOEC < 0.03 mg/L	*Selenastrum capricornutum* (green algae) growth Vos Algal Assay Procedure - Bottle Test

*Value above the solubility limit

Available chronic toxicity endpoints indicate that HCB affects reproduction in aquatic invertebrates and growth in algae. Two of the endpoints are above the water solubility of the chemical and correspond to the amount of HCB added to the test medium. However, the organisms were likely to be only exposed to HCB at the water solubility limit (0.006 mg/L) as no solvent was used to enhance solubility in the study (Calamari et al. 1983). No acceptable long term toxicity data for HCB were found for fish.

Effects on terrestrial Life

HCB shows toxic effects in birds and mammalian predators exposed to the chemical through diet.

Quail (*Coturnix japonica*) fed diets containing HCB over 90 days showed increased mortality and significantly reduced hatchability at exposure of 100 µg/g at 20 µg/g, respectively. At exposures of 5 µg/g, liver damage was observed (Vos et al. 1971).

Mink (*Mustela vison*) fed HCB in diet showed increased adult mortality and adverse reproductive effects at exposure of 125 mg/kg diet. Decreased litter sizes, increased still births and kit mortality and slower progeny growth were all observed in animals fed HCB (Bleavins et al. 1984).

Endocrine effects/activity

The chemical binds to the aryl hydrocarbon (Ah) receptor, and can alter endocrine (i.e. thyroid hormone levels) and reproductive organs, which may result in developmental, neurological and teratogenic effects (Barber et al. 2005).

Predicted no-effect concentration (PNEC)

The PNEC is not estimated since an acceptable concentration threshold for persistent organic pollutants cannot be determined with any degree of certainty.

Categorisation of environmental hazard

The chemical is a POP according to its listing under Annexes A and C of the Stockholm Convention.

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

Persistence

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

Adverse effects

Based on available ecotoxicity values in aquatic organisms, and evidence of adverse reproductive effects in higher predators after exposure in diet, HCB 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, the chemical meets the Annex D criteria for LRT.

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