2.4 Hazard assessment for endpoints of concern

2.4.1. Toxicity

Toxicokinetics

Toxicokinetic studies with rats show that after an oral dose, the substance is distributed to the blood and tissues (Umegaki et al., 1993; ICCA/WCC, 2007 citing Thomas and coauthors). Linder et al., (1980) observed that rats fed with PeCB accumulated approximately 1.5 – 2.2 times the dietary concentration in their adipose tissues. Umegaki et al., (1993) studied the kinetics of PeCB in blood and tissues of rats given a single oral dose by gavage of either 15 mg or 20 mg. PeCB was observed in the blood, liver, kidney, brain, and fat tissue as well as in the feces (4.8% of the dose). In the blood, also the major metabolite pentachlorophenol was observed.

Den Besten et al (1994) studied the urinary metabolite profile of PeCB in the rat after dietary exposure for 13 weeks. PeCB was metabolized to the major metabolites pentachlorophenol (PCP), 2,3,4,5-tetrachlorophenol (TCP), mercaptotetrachloro-phenol (MTCP), the glucuronide derivative of pentachlorothiophenol (PCTP), and the minor metabolites tetrachlorohydroquinone (TCHQ), methylthiotetrachlorophenol (MeTTCP), hydroxytetrachlorophenyl sulphoxide (HTCPS), and bis(methylthio)-trichlorophenol (bis-MeTTriCP). The study also revealed that oxidation of PeCB to 2,3,4,5-TCP was not mediated by cytochrome P450IIIA. In the urine of rabbits exposed to a single oral dose of PeCB, also pentachlorophenol and 2,3,4,5-tetrachlorophenol was observed (Slooff et al., 1991, citing Kohli et al., 1976).

A study with coyotes showed that PeCB is excreted in the faeces (Johnston et al., 1997). Coyotes were dosed with PeCB (single dose of 130, 260 or 520 mg). In both studied matrices, faeces and adipose tissue, residues of PeCB were determined. PeCB was detectable in faeces for six months post-dosing. In the faeces, also the metabolites pentachlorophenol and 2,3,4,5-tetrachlorophenol were detected.

Data on other than the oral exposure route are limited available. WHO-ICPS (1991) indicates that the chlorobenzenes are less readily absorbed through the skin, but that levels of the same isomer of the chlorobenzenes in various tissues appear to be similar, regardless of the route of administration. The ingestion of a lethal dose leads to respiratory paralysis, while the inhalation of high doses causes local irritation and depression of the central nervous system WHO-ICPS (1991).

Acute toxicity

PeCB has been tested on rats and mice. Results of acute toxicity tests are available for oral and dermal exposure (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). LD_{50}s for PeCB (by gavage in peanut oil) are 940 to 1125 mg/kg bw in adult and weanling rats and 1175 and 1370 mg/kg bw in Swiss Webster mice (Linder et al., 1980 cited in Government of Canada, 1993). Decreased activity and tremors were observed in both species at sublethal doses; the kidneys, liver and adrenal glands of rats were also enlarged. In some rats, the gastric mucosa was hyperaemic, and a slight reddish fluorescence of the gastrointestinal tract was observed in both rats and mice under ultraviolet light, suggesting porphyria (Government of Canada, 1993). In the study of Allen et al., (1979, cited in Slooff, 1991), a LD50 of 250 mg/kg bw was observed in rats. Ariyoshi et al., (1975, cited in Slooff, 1991) observed an increase of cytochrome P450 content in rats as well as an increase in the activity of two hepatic enzymes after oral administration of 250 mg/kg bw once daily during 3 days.

To determine a dermal LD50 one concentration (i.e., 2500 mg/kg bw) was tested on rats, but no toxic effects were seen at this dose (Linder et al., 1980 cited in Slooff, 1991). Based on this study, a NOEC of > 2500 mg/kg bw can be established for dermal exposure.

PeCB is classified in the European ESIS database as R22, harmful if swallowed (European Chemicals Bureau, 2007). WHO-IPCS (1991) reported that data on skin and eye irritation potential and on sensitization potential were mainly restricted to 1,2,4-trichlorobenzene. No data were available for PeCB.

Subchronic toxicity

PeCB has been tested on rats and mice. Results of (sub)chronic toxicity tests are available for dietary exposure, see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21. In female Sherman rats ingesting diets containing 500 mg/kg and greater (> 37.5 mg/kg bw/day) PeCB for 100 days, there was an increase in liver weight and hypertrophy of hepatic cells (Linder et al., 1980). There was also an increase in kidney weights and renal hyaline droplet formation in males at exposure levels ≥125 mg/kg (equivalent to ≥8.3 mg/kg bw/day). In addition, at 1 000 mg/kg (equivalent to 81.1 mg/kg bw/day for males and 78.7 mg/kg bw/day for females), the effects observed were: an increase in adrenal weight and focal areas of renal tubular atrophy and interstitial lymphocytic infiltration in males; an increase in kidney weight in females; a decrease in haemoglobin and an increase in white blood cells in both sexes; and decreases in red blood cells and haematocrit in males. The no-observed-effect-level (NOEL) in female rats, derived on the basis of the results of this study, was 250 mg/kg (equivalent to 18.2 mg/kg bw/day); the lowest-observed-effect-level (LOEL) in males was 125 mg/kg (equivalent to 8.3 mg/kg bw/day) (calculations by Government of Canada, 1993).

In a study of NTP (1991) rats and mice were exposed to PeCB through their diet. Observed effects were among others: decreases in the mean body weights of male rats at exposure levels ≥ 1 000 mg/kg diet and in females at all concentrations (≥ 33 mg/kg), increase in absolute and relative liver weights (33 mg/kg in males), centrilobular hepatocellular hypertrophy (as low as 330 mg/kg for males), increases in kidney weights and renal histopathological effects at concentrations as low as 100 mg/kg, nephrotoxic effects in females (≥ 1 000 mg/kg), increase of the concentration of protein in the urine in male and female rats at ≥ 1 000 mg/kg, decrease of free thyroxin and total thyroxin concentrations in male and female rats indicating moderate hypothyroxinemia and abnormalities were observed at concentrations of ≥330 mg/kg in females and ≥ 1 000 mg/kg in males. The incidence of abnormal sperm in males was also increased at both dietary concentrations at which it was examined (330 and 2 000 mg/kg). On the basis of histopathological lesions, the authors considered the NOELs to be 33 mg/kg in male rats and 330 mg/kg in females (approximately 2.4 and 24 mg/kg bw/day, respectively) (calculations by Government of Canada, 1993).

In PeCB exposed mice in the same study NTP (1991), observed effects were among others: ventral swelling and ruffled fur (2 000 mg/kg), increase of kidney weights (≥330 mg/kg in males), functional effects on the thyroid at all concentrations in both sexes (≥33 mg/kg), increase in liver weights (at 100 mg/kg in males). The only exposure-related histological lesion in mice of either sex was centrilobular hepatocellular hypertrophy and minimal necrosis, observed at all concentrations in males and at ≥ 330 mg/kg (equivalent to 68 mg/kg bw/day) in females. On the basis of the histopathological lesions, the authors considered the NOEL in female mice to be 100 mg/kg (approximately 22 mg/kg bw/day). No NOEL for males could be established (LOEL = 33 mg/kg or approximately 5.2 mg/kg bw/day) (calculations by Government of Canada, 1993).

In contrast to ingestion, WHO-ICPS (1991) does not provide data on dermal exposure and inhalation of PeCB, which indicates that such data are limited. The lowest NOELs reported for the ingestion of PeCB were between 2.4 and 24 mg/kg per day. Ingestion of high doses by rats and mice resulted in hepatic and renal toxicity.

Mutagenicity and carcinogenicity

Epidemiological studies of exposed populations are not available and information on carcinogenicity in experimental animals has not been identified. PeCB showed no genotoxicity in a small number of *in vitro* and *in vivo* studies of a limited range of investigated genetic endpoints.

PeCB has been tested negative in the Ames test (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). Based on limited available data, mutagenicity in *S. typhimurium* with and without metabolic activation, effects on chromosomes in Chinese Hamster ovary cells *in vitro,* and micronuclei in peripheral blood smears in animals from the NTP sub-chronic study, PeCB has been assessed as not genotoxic (Haworth et al., 1983 and NTP, 1991 cited in Government of Canada, 1993). Several studies (Thomas et al., 1998 and Gustafson et al., 2000; Ying et al., 2001) investigated the tumor-promoting activity in medium term carcinogenicity assays of various chlorobenzene isomers including PeCB. The results suggest that PeCB promotes glutathione *S*-transferase (GSTP1-1) positive preneoplastic foci formation in rat liver, following diethylnitrosamine (DEN) initiation.

Both Health Canada and U.S. EPA have reviewed the cancer toxicity data of PeCB. The cancer weight-of-evidence classification is based on all routes of exposure. Neither group derived a risk value. Both groups concluded that the substance is unclassifiable with respect to its carcinogenicity in humans due to the lack of data. PeCB is not classified as a carcinogen by IARC or by the EU (European ESIS database).

Reproductive and developmental toxicity
Available studies concerning the embryotoxicity, foetotoxicity and teratogenicity of PeCB include one study in rats (and one in mice (Villeneuve and Khera, 1975 and Courtney et al., 1977, cited in Government of Canada, 1993) (see Table 2.6, Annex II, UNEP/POPS/POPRC.3/INF/21). Results of the study of Villeneuve and Khera (1975) indicated that PeCB is foetotoxic (an increased incidence of extra ribs and sternal defects was observed in the offspring) at maternal exposure doses of 50 mg/kg bw/day. The exposure concentration was below the concentration that induced toxic effects in the mothers. In mice, no embryotoxic, foetotoxic or teratogenic effects were observed in the offspring at doses which were maternally toxic (50 mg/kg bw/day and above)(Courtney et al., 1977). In the only identified study on reproductive toxicity of PeCB, Linder et al. (1980) reported that suckling pups of PeCB treated mothers fed ≥ 250 mg/kg developed tremors (LOAEL = 18.2 mg/kg/day). At 1000 mg/kg, most sucklings died before weaning.

The studies above are also cited in WHO-ICPS (1991) who conclude that there is some evidence that the higher chlorinated benzenes (TCBs, TeCBs, PeCB) are embryotoxic or fetotoxic at dose levels that are not maternally toxic. WHO-ICPS (1991) also remark that the available data are not consistent and that the toxicities of the various isomers of the TCBs and TeCBs for the mother and fetus vary considerably. Most reported effect (NOAEL, NOEL) and no effect levels (LOAEL, LOEL) vary between 17 and 200 mg/kg PeCB per day.

PeCB showed high oral toxicity with LD50 doses as low as 250 mg/kg bw in rats. From the limited data available, dermal LD50s are higher. Data on skin and eye irritation potential and on sensitization potential are limited. In contrast to ingestion, WHO-ICPS (1991) does not provide data on dermal exposure and inhalation of PeCB, which indicates that such data are limited. The lowest NOELs reported for the ingestion of PeCB were between 2.4 and 24 mg/kg bw per day. Ingestion of high doses by rats and mice resulted in hepatic and renal toxicity.

PeCB showed no genotoxicity in a small number of *in vitro* and *in vivo* studies of a limited range of investigated genetic endpoints. Data on mutagenity and carcinogenity are limited. Both Health Canada and US-EPA concluded that the PeCB is unclassifiable with respect to its carcinogenicity in humans due to the lack of data. PeCB is not classified as a carcinogen by IARC, nor by the EU (European ESIS database). There is some evidence that PeCB is embryotoxic or fetotoxic at dose levels that are not maternally toxic.

2.4.2. Ecotoxicity

Aquatic toxicity
Acute and chronic toxicity data are available for both freshwater (see Table 2.7, Annex II, UNEP/POPS/POPRC.3/INF/21) and marine organisms (see Table 2.8, Annex II, UNEP/POPS/POPRC.3/INF/21). The lowest acute toxicity values are 100 µg/L for freshwater fish species (EC50) and 87 µg/L for a marine crustacean (LC50). The lowest chronic values (NOECs) are 2 µg/L for a freshwater fish and 14 µg/L for a marine crustacean. According to these findings, species sensitive to PeCB can be found in both the freshwater and the marine environment.

Within the European Union PeCB is classified as a substance which is very toxic to aquatic organisms and which may cause long-term adverse effects in the aquatic environment (Risk phrases N; R50 and R53) (European Chemicals Bureau, 2007). This classification is based on the fact that the substance is very toxic to fish, daphnia or algae (LC50 ≤1 mg/L) and the substance is not readily degradable or bioaccumulative.

Soil and sediment toxicity
Limited data are available for soil and sediment. Tests with various chlorobenzenes were carried out by Van Gestel et al (1991). Two earthworm species were raised on a natural sandy soil (KOBG) and an artificial OECD standard soil. Average LC50 values varied between 115 and 238 mg/kg dry weight, whereas LC50 values in pore water varied between 55.1-117.7 µg/L. Van Gestel et al (1991) concluded that based on pore water concentrations earthworms are more sensitive to PeCB than fish, but that this may be due to differences in test design.

Only one study on the toxicity of PeCB in plants was identified. Duplicate tests were carried out in which *Lactuca sativa* seedlings were grown on OECD soil contaminated with PeCB. The seedlings were harvested after 7 and 14 days. EC50 values varied between 56 and 862 mg/kg dw (Hulzebos et al. 1993). Experiments in solution resulted in an EC50 value of ±1.0 mg/L. Details of the tests are provided in Table 2.9, Annex II, UNEP/POPS/POPRC.3/INF/21.

Toxicity to birds
No toxicity data on birds are available for PeCB.

Multiple chemicals and toxicological interactions
Annex E request information on toxicological interactions involving multiple chemicals (Annex E, b). Limited information is available on this subject. Yoo et al (2003) report on their studies on the kinetics of PeCB: "The kinetics and toxicity of pentachlorobenzene were assessed using a freshwater (*Hyalella azteca*) and marine amphipod (*Leptocheirus plumulosus*). The results of these studies demonstrated the additive toxicity of PeCB with other organic chemicals (pyrene)."

Comparison of exposure and effect data
Several methods, exposure routes and species with very different feeding strategies were used by ICCA/WCC to determine the lethal and critical body burden of PeCB. Based on the general knowledge on substances with a narcotic mode of action and the available data on PeCB, such as the *Hyalella* growth/mortality study and other information discussed, an estimation of 25 mg/kg PeCB/kg (0.1 mmol) was tentatively proposed by ICCA/WCC (2007) as a Critical Body Burden for chronic effects.

A very recent publication of Schuler et al (2007b) has reported critical whole body residues of pentachlorobenzene of 58 mg/kg and 5 mg/kg for *Hyalella azteca* and *Chironomus tentans* respectively. These residue levels are lower than the highest concentrations reported for temperate regions in Table 2.5 in the Annex POPRC3/INF21 and 150-1500 times higher than the highest values of <0.1 – 37 µg/kg wet weight in biota reported for the Faroe Islands by Hoydal and Dam (2003). Other concentrations reported from remote areas are of the same order of maginitude, e.g. Adelie penguin eggs (Antartic) contained 0.68 µg/kg ww (Corsolini et al., 2006) and whole body concentrations from fish in the White Sea were up to 5 µg/kg ww (ICCA/WCC, 2007 citing Muir et al., 2003).

The World Chlorine Council (ICCA/WCC, 2007) has provided information related to two other approaches. The first approach focused on PeCB organic carbon concentrations in sediments from Canadian lakes and showed that in both rural and remote sites, PeCB organic carbon concentrations were 410-75000 times lower than Environment Canada's "estimated no effect value" for freshwater benthic organisms. In the second approach, comparisons were made between exposure estimations for a pisciverous predator and for polar bear using assumptions considered by the WCC as "worst case assumptions", and effect levels derived from human Reference Dose and Tolerable Daily Intakes from USA and Canada. These estimations of exposure were 13 and 20 times lower than the derived effect levels, respectively.

The available information has not been sufficient for confirming if the values given above represent real critical body burdens or just expressions of internal dose or whole body residues levels. Both concepts have fundamental differences related to the understanding of the mechanism of action of the chemical. Nevertheless, it should be noted that expressing the toxicological effects as internal dose or, whenever possible, critical body burdens, improves the effect assessment but only reduces partially its uncertainty. In addition, all the uncertainty related to the exposure assessment remains. While monitoring levels above critical body burdens or internal toxic doses clearly indicate a risk, the fact that current measured concentrations are below these triggers should in no case be interpreted as a confirmation of the absence of risk, particularly in the assessment of POPs and POPs candidates.

3 Synthesis of the information

Pentachlorobenzene is a chlorinated organic compound. According to available data, pentachlorobenzene should be considered as persistent given the considerable number of estimated and experimental half-lives in atmosphere, soils, sediments, and water. Persistence in the environment depends on the rate of photo-oxidation, the presence of oxygen and organic matter. Pentachlorobenzene meets the criterion on bioaccumulation. BCF values for pentachlorobenzene range from 1085 – 23 000 L/kg for fish, 833 – 4 300 L/kg for mollusca, and 577 – 2258 L/kg for crustacean. Biomagnification may be expected due to the high $\log K_{ow}$ and the fact that biotransformation is insignificant. However, data on the biomagnification of pentachlorobenzene are lacking.

The available data support the potential for long range transport of pentachlorobenzene. The physical and chemical characteristics are within the range of the other POPs. Model estimations on the transport distance resulted in distances of 8 000 km, while estimates based on air measurements suggested 13 338 km. Monitoring data also indicate that PeCB is subject to long range transport. PeCB was detected in air and precipitation at various locations in the world, many of those

far from its sources. The small spatial variability across the Northern Hemisphere observed in some studies also indicate that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global hemisphere.

A large quantity of monitoring data exists on PeCB detected in abiotic matrices as well as in biota in temperate zones, mainly originating from developed countries. In general, concentrations of PeCB in the temperate zones of the world seem to be decreasing. This pattern is representative for most POPs. For the Arctic and Antarctic area, only recent data are available which do not enable a trend to be derived.

Case reports of adverse effects in individuals, or epidemiological studies of populations exposed to PeCB have not been identified. The only risk phrase for pentachlorobenzene in the European ESIS database is R22, harmful if swallowed. Lowest LD50 observed for acute exposure was 250 mg/kg bw. Repeat-dose mammalian toxicity tests result in evidence of hepatic, nephric, hematological, and developmental toxicity for this chemical. According to the American Hazardous Substances Data Bank pentachlorobenzene is not classifiable as to human carcinogenicity because there are no human data and no animal data available. PeCB is moderately toxic to humans. Pentachlorobenzene is very toxic to aquatic organisms and may cause long-term adverse effects in the aquatic environment. Data on soil and sediment organisms are limited or lacking.

Bioavailability of pentachlorobenzene is inversely proportional to the organic carbon content of the soil or sediment. However, experiments suggest that hydrophobic chemicals bound to the sediment or suspended sediment may act as a reservoir and result in continuous uptake. There are limited quantitative data on this process for pentachlorobenzene.

The data from Europe and North America show that production and use of pentachlorobenzene has ceased over the last decades, but it cannot be excluded that PeCB is produced or used elsewhere. Unintentional release of pentachlorobenzene as a byproduct of incomplete combustion appears to be the largest current source. However, this conclusion is based on data for Europe and North America only.

An important element in the assessment of the potential risk of PeCB is the assessment of the risk associated with intended and non-intended uses. This distinction is not possible with the current information but it should be very useful for the decision making process. Such an analysis would request precise information on the amounts released by intentional production and use in the past and the unintentional releases plus a correction for the degradation rate of the substance after release. Data on past production and use are currently lacking.

PeCB meets all screening criteria on long range transport, persistence, bioaccumulation and toxicity. Generally, environmental concentrations seem to be decreasing. Production and use have ceased in Europe and North America, but data from other parts of the world are limited. Unintentional release as a byproduct of incomplete combustion appears to be the most important source of PeCB in the environment.

The available information does not allow the Committee to distinguish between the environmental burden caused by intentional use and the burden caused by the unintentional production and releases of PentaCB. Clarifying this distinction would help the Committee to prepare the risk management evaluation and to formulate its final conclusions. Hence, additional data on this issue should be sought.

4 Concluding statement

PeCB is persistent in the environment and is bioaccumulative. The small spatial variability in the ranges of air concentrations across the Northern Hemisphere indicates that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global hemisphere. There are monitoring data from remote areas, backed up by modelling results that suggest that pentachlorobenzene can be transported over great distances. Pentachlorobenzene is moderately toxic to humans, but is very toxic to aquatic organisms.

As a result of the long range transport of PeCB, neither a single country nor a group of countries alone can abate the pollution caused by this substance. Unintentional release of PeCB, as a byproduct of incomplete combustion, appears to be the largest current source. Measures to reduce these releases can only be taken at a global scale. Although the production and use of pentachlorobenzene seems to have ceased in most countries, its reintroduction remains possible. This could lead to increased releases and levels in the environment. Based on the available evidence, PeCB is likely, as a result of its long

range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

As the distinction between the environmental burden caused by intentional use and the burden caused by unintentional production and releases would support the preparation of the risk management evaluation and making the final recommendation, the Committee considers that an additional effort should be made to fill this gap.

References

Aarnoutse PJ, De Jong APJM, Beurskens JEM. Analysis of dichloro benzene in porewater and sediment from the lake 'Ketelmeer' [in Dutch]. Bilthoven, the Netherlands: RIVM, 1996. Report 502501041.

Adrian L, Görisch H. Microbial transformation of chlorinated benzenes under anaerobic conditions. Research in Microbiology 2002;153:131-137.

Åkerblom N (2007) The importance of Sorption and Uptake Routes. Ph D Thesis University of Uppsala

Aracil I, Font R, Conesa JA. (2005) Semivolatile and volatile compounds from the pyrolysis and combustion of polyvinyl chloride. J. Anal and Appl Pyrolysis 74:465-478

ATSDR (2007). The Agency for Toxic Substances and Disease Registry. http://www2.atsdr.cdc.gov/gsql/sitecontam.script, http://www2.atsdr.cdc.gov/gsql/getsite.script?in_cas=000608-93-5

Banerjee S, Sugatt RH, O'Grady DP. 1984. A simple method for determining bioconcentration parameters of hydrophobic compounds. Environ. Sci. Technol. 18, (2), 79-81.

Barrows ME, Petrocelli SR, Macek KJ, Carroll JJ. 1980. Bioconcentration and elimination of selected water pollutants by bluegill sunfish (Lepomis macrochirus). In: Haque R, ed. Dynamics, exposure and hazard assessment of toxic chemicals. Ann Arbor, Michigan, U.S.A.: American Chemical Society. p. 379-392.

Belfroid, A., van der Aa, E. and Balk, F. 2005. Addendum to the risk profile of Pentachlorobenzene. Royal Haskoning report 9R5744.01/R0005/ABE/CKV/Nijm.

Beurskens JEM, Dekker CGC, Jonkhoff J, Pompstra L. Microbial dechlorination of hexachlorobenzene in a sedimentation area of the Rhine River. Biogeochemistry 1993;19:61-81.

Beurskens JEM, Dekker CGC, Van den Heuvel H, Swart M, De Wolf J, Dolfing J. Dechlorination of chlorinated benzenes by an anaerobic microbial consortium that selectively mediates the thermodynamic most favorable reactions Environmental Science & Technology 1994;28:701-706.

Boer, J. de, Van der Zande, T.E., Pieters, H., Ariese, F., Schipper, C.A., van Brummelen, T. Vethaak, A.D., 2001. Organic contaminants and trace metals in Flounder liver and sediment from the Amsterdam and Rotterdam harbours off the Dutch coast. J Environ Monitoring Aug;3(4):386-393.

Borghini F, Joan O. Grimalt, Juan C. Sanchez-Hernandez and Roberto Bargagli. 2005. Organochlorine pollutants in soils and mosses from Victoria Land (Antarctica). Chemosphere 58: 271-278.

Beck J, Hansen K. The degradation of Quintozene, Pentachlorobenzene, Hexachlorobenzene and Pentachloroaniline in soil. Pesticide Science 1974;5:41-48.

Bro-Rasmussen F, Noddegaard E, Voldum-Clausen K. Comparison of the disappearance of eight Organophosphorus insecticides from soil in laboratory and in outdoor experiments. Pesticide Science 1970;1:179-182.

Calambokidis, J, Jeffries, S, Ross PS and Ikonomou M. (1999). Temporal trends in contaminants in Puget sound harbor seals. US EPA and Puget Sound Water Quality Action Team.

Cornelissen G, Gustafsson Ö. The role of environmental black carbon in sediment sorption and bioavailability. Stockholm: Institute for Applied Environmental Research (ITM), Stockholm University, 2004. http://ipimar-iniap.ipimar.pt/Vale/oral%20presentations%204.pdf

Carlson AR, Kosian PA. 1987. Toxicity of chlorinated benzenes to fathead minnows (Pimephales promelas). Arch. Environ. Contam. Toxicol.; 16, 129-135.:

Chaisuksant Y, Yu Q, Connell DW. 1997. Bioconcentration of bromo- and chlorobenzenes by fish (Gambusia affinis). Water Res 31: 61-68.

CHEMFATE Database; Environmental Fate Data Base (EFDB) at Syracuse Research Centre. Available at: http://www.syrres.com/esc/efdb.htm

Corsolini, S., Covaci, A., Ademollo, N., Focardi, S., Schepens, P. 2006. Occurrence of organochlorine pesticides (OCPs) and their enantiomeric signatures, and concentrations of polybrominated diphenyl ethers (PBDEs) in the Adélie penguin food web, Antarctica Environ Pollution 140(2): 371-382.

Den Besten C, Bennik MMH, Van Iersel M, Peters MAW, Teunis C, van Bladeren PJ. 1994. Comparison of the urinary metabolite profiles of hexachlorobenzene and pentachlorobenzene in the rat. Chem Biol Interact 90:121–137.

Environment Canada 2005. Risk management strategy for Pentachlorobenzene (QCB) and tetrachlorobenzenes (TeCBs). Available at: http://www.ec.gc.ca/Toxics/docs/substances/certToxics/rms/EN/CBz_RMS_E_05-01-05.pdf

European Chemicals Bureau (2007). ESIS (European Substances Information System). http://ecb.jrc.it/esis/ Accessed on March 22.

http://ec.europa.eu/food/plant/protection/evaluation/existactive/list1-19_en.pdf

European Commission. (2007). Community Implementation Plan for the Stockholm Convention on Persistent Organic Pollutants. SEC(2007)341. http://www.pops.int/documents/implementation/nips/submissions/SEC_2007_341.pdf

Gabrielsen, G.W., Knuden, L.B., Verreault, J., Pusk, K., Muir, D.C., Letcher, R.J., 2004. Halogenated organics contaminants and metabolites in blood and adipose tissue of polar bears (Ursus maritimus) from Svalbard. SFT project 6003080. Norsk Polar Institut. SPFO report 915/2004.

Geyer H, G. Politzki, D. Freitag. 1984. Prediction of ecotoxicological behaviour of chemicals: Relationship between n-octanol/water partition coefficient and bioaccumulation of organic chemicals by alga Chlorella. Chemosphere, 13, (2), 269-284.:

Gobas FAPC, McNeil EJ, Lovett-Doust L, Haffner GD. 1991. Bioconcentration of chlorinated aromatic hydrocarbons in aquatic macrophytes. Environ Sci Technol 25: 924-929.

Government of Canada. 1993. Canadian Environmental Protection Act Priority Substances List Assessment Report: Pentachlorobenzene. Environment Canada and Health Canada, Ottawa, Ontario. 32 pp. Available at: http://www.hc-sc.gc.ca/ewh-semt/pubs/contaminants/psl1-lsp1/pentachlorobenzene/index_e.html

Government of Canada (2003). Follow-up Report on Five PSL1 Substances for Which There Was Insufficient Information to Conclude Whether the Substances Constitute a Danger to the Environment 1,2-Dichlorobenzene, 1,4-Dichlorobenzene, Trichlorobenzenes, Tetrachlorobenzenes, Pentachlorobenzene. Available at: http://www.ec.gc.ca/substances/ese/eng/psap/assessment/PSL1_chlorobenzenes_followup.pdf

Grimalt, JO, F Borghini, JC Sanchez-Hernandez, R Barra, CJ Torres Garcia, S Focardi. 2004. Temperature Dependence of the distribution of Organochlorine compounds in the mosses of the Andean Mountains. Environ. Sci. Technol. 38: 5386-5392.

Gustafson, DL, Long ME, Thomas RS, Benjamin SE, Yang RSH. 2000. Comparative hepatocarcinogenicity of hexachlorobenzene, pentachlorobenzene, 1,2,4,5-tetrachlorobenzene, and 1,4-dichlorobenzene: application of a medium-term liver focus bioassay and molecular and cellular indices. Toxicol. Sci. 53: 245-252

Hesse JM, Speijers GJA, Taalman RDFM (1991). Appendix to Report no. 710401005 Integrated criteria document chlorobenzenes. Effects. RIVM, Appendix to Report no. 710401005.

Hoogen G Van, Opperhuizen A. 1988. Toxicokinetics of chlorobenzenes in fish. Environ. Toxicol. Chem. 7, 213-219.

Hoydal, K, Dam, M (2003) AMAP Greenland and the Faroe Islands 1997-2001. Vol. 3: The Environment of the Faroe Islands. DANCEA, Danish Cooperation for Environment in the Arctic Ministry of Environment.

HSDB (2003). U.S. National Library of Medicine, Hazardous Substances Data Bank, HSDB. Information on pentachlorobenzene. http://toxnet.nlm.nih.gov/cgi-bin/sis/search/r?dbs+hsdb:@term+@rn+@rel+608-93-5

Hulzebos EM, Adema, DMM, Dirven-Van Breemen EM, Henzen, L, Van Dis WA, Herbold HA, Hoekstra JA, Baerselman R and Van Gestel CAM. (1993). Phytotoxicity studies with Lactuca sativa in soil and nutrient solution. Env. Toxicol. Chem. 12: 1079-1094.

ICCA/WCC, International Council of Chemical Associations/World Chlorine Council (2007). ICCA-WCC Submission for PeCB & All Risk Profiles for the POPs Review Committee of the Stockholm Convention including annexes.

IUPAC-NIST solubility database. Available at: http://srdata.nist.gov/solubility/

Johnston JJ, Furcolow CA, Kimball BA. 1997. Identification of Metabolites of Pentachlorobenzene and 1,2,4,5-Tetrachlorobenzene in Coyote Feces: Development of Physiological Markers for Wildlife Damage Control. Pestic. Sci. 1997, 50, 249-257

Kaj, L., Dusan, B., 2004. Screening av Organiska Moljoegidter I Fisk-HCBD och Klorenbensener. (Screening of organics environmental toxins-HBCD and chlorobenzenes.). Report B1557, Swedish Environmental Research Int. (IVL), Stockholm, Sweden.

Kim KS, Hong KH, Ko YH, Kim MG. (2004). Emission characteristics of PCDD/Fs, PCBs, chlorobenzenes, chlorophenols, and PAHs from polyvinylchloride combustion at various temperatures. J Air Waste Manag Assoc. 54(5):555-562

King, TL, Lee, K, Yeats, P, Alexander, R. (2003). Chlorobenzenes in Snow Crab (Chionoectes opilio): Time-series monitoring following an accidental release. Bull. Environm. Contam. Toxicol. 71: 543-550.

Klimisch HJ, Andreae M, Tillman U. 1997. A systematic approach for evaluating the quality of experimetnal toxicological and ecotoxicological data. Regul Toxicol Pharmacol 25: 1-5.

Landrum PF, Steevens JA, Gossiaux DC, McElroy M, Robinson S, Begnoche L, Chernyak S, Hickey J. 2004. Time-dependent lethal body residues for the toxicity of pentachlorobenzene to Hyalella azteca. Environ Toxicol Chem 23: 1335-1343.

Legierse KCHM, Sijm DTHM, Van Leeuwen CJ, Seinen W, Hermens JLM. 1998. Bioconcentration kinetics of chlorobenzenes and the organophosphorus pesticide chlorthion in the pond snail Lymnaea stagnalis - a comparison with the guppy Poecilia reticulata. Aquat Toxicol 41: 301-323.

Linder, R., T. Scotti, J. Goldstein, K. McElroy, and D. Walsh. 1980. Acute and subchronic toxicity of pentachlorobenzene. J. Environ. Pathol. Toxicol., 4(5-6): 183-196.

Lunde, G., Bjorseth, A. (1977). Human blood samples as indicators of occupational exposure to persistent chlorinated hydrocarbons. Sci. Total Environm. 8(3): 241-246.

Lydy MJ, Belden JB, Ternes, MA. (1999). Effects of temperature on the toxicity of M-Parathion, Chlorpyrifos, and Pentachlorobenzene on Chironomus tentans. Arch. Environ. Contam. Toxicol. 37: 542-547.

Mackay D, Shiu W-Y, Ma K-C, Lee SC. 2006. Physical-chemical properties and environmental fate for organic chemicals. 2nd ed. Boca Raton, FL, U.S.A.: CRC Press, Taylor & Francis Group. 4182 pp.

Mantseva E, S Dutchak, O Rozovskaya, V Shatalov. 2004. EMEP contribution to the preparatory work for the review of the CLRTAP Protocol on Persistent Organic Pollutants. EMEP MSC-E Information Note 5/2004. Meteorological Synthesizing Centre –East, Moscow, Russia.

Masunaga S, Susarla S, Yonezawa Y. Dechlorination of chlorobenzenes in anaerobic estuarine sediment. Water Science and Technology 1996;33:173-180.

Ministry of the Environment of Ontario (1999). Niagara river mussel biomonitoring program 1997.

Ministry of the Environment of Ontario (2003). Niagara river mussel biomonitoring program 2000.

Mortimer MR, Connell DW. 1993. Bioconcentration factors and kinetics of chlorobenzenes in a juvenile crab [Portunus pelagicus (L)]. Aust J Mar Freshwater Res 44: 565-576.

Mortimer MR, Connell DW. 1995. Effect of exposure to chlorobenzenes on growth rates of the crab Portunus pelagicus (L). Environ Sci Technol 29:1881–1886.

Muller J, Dongmann G, Frischkorn CGB. (1997). The effect of aluminium on the formation of PAH, methyl-PAH and chlorinated aromatic compounds during thermal decomposition of PVC. Journal Anal and Appl Pyrolysis 43:157 – 168.

NITE (2007). (Japan, National Institute of Technology and Evaluation) at: http://www.safe.nite.go.jp/english/db.html. accessed March 17 2007.

NTP (National Toxicology Program) (1991). NTP report on the toxicity studies of Pentachlorobenzene in F344 rats and B6C3F1 mice (feed studies). NTP Tox 6. US Department of Health and Human Services, RTP, North Carolina. available through (http://ntp.niehs.nih.gov/index.cfm?objectid=072C8956-036B-A0CA-51A7A8D30E5E7BDA)

Oliver BG, Niimi AJ. 1983. Bioconcentration of chlorobenzenes from water by rainbow trout: correlations with partition coefficients and environmental residues. Environ. Sci. Technol.; 17, 287-291.:

OSPAR Commission for the protection of the marine environment of the North-East Atlantic (1998) OSPAR Strategy with regard to Hazardous Substances http://www.ospar.org/eng/html/sap/strategy_hazardous_substances.htm

PHYSPROP Database; Environmental Fate Data Base (EFDB) at Syracuse Research Centre. Available at: http://www.syrres.com/esc/efdb.htm

Priority Substance No. 26. Pentachlorobenzene. Substance Data Sheet. (2005). Environmental Quality Standards (EQS). Brussels: EU Common Implementation Strategy for the Water Framework Directive.

Ramanand K, Balba MT, Duffy J. Reductive dehalogenation of chlorinated benzenes and toluenes under methanogenic conditions. Applied and Environmental Microbiology 1993;59:3266-3272.

Renberg L, M. Tarkpea, E. Linden. 1985. The use of the bivalve Mytilus edulis as a test organism for bioconcentration studies. Ecotoxicol. Environ. Saf. 9, 171-178.

Ribes A, Grimalt JO, Torres Garcia CJ, Cuevas E. (2002). Temperature and organic matter dependence of the distribution of organochlorine compounds in mountain soils from the subtropical Atlantic (Teide, Tenerife Island). Environ Sci Technol. 236(9):1879-85.

Rossberg et al., (2006). Ullmann's Encyclopedia of Industrial Chemistry.

Scheunert I, Topp E, Schmitzer J, Klein W, Korte F. Formation and fate of bound residues of [14C]benzene and [14C]chlorobenzenes in soil and plants Ecotoxicology and Environmental Safety 1985;9:159-170.

Schuler LJ, Landrum PF, Lydy MJ. (2006). Comparative toxicity of fluoranthene and pentachlorobenzene to three freshwater invertebrates. Environ Toxicol Chem 25: 985-994

Schuler LJ, Landrum PF, Lydy MJ. 2007. Response spectrum of fluoranthene and pentachlorobenzene for the fathead minnow (Pimephales promelas). Environ Toxicol Chem 26: 139-148.

Schuler, LJ, Landrum, PF, Lydy MJ. (2007b). Response spectrum of pentachlorobenzene and fluoranthene for Chironomus tentans and Hyalella azteca. Env. Toxicol. Chem. 26(6): 1248-1257.

Shen, L, F Wania, YD Lei, C Teixeira, DCG Muir, TF Bidleman. 2005. Atmospheric distribution and long-range transport behaviour of organochlorine pesticides in North America. Environ. Sci. Technol. 39: 409-420.

Shen H, Main KM, Virtanen HE, Damggard IN, Haavisto AM, Kaleva M, Boisen KA, Schmidt IM, Chellakooty M, Skakkebaek NE, Toppari J, Schramm KW. (2007). From mother to child:Investigation of prenatal and postnatal exposure to persistent bioaccumulating toxicants using breast milk and placenta biomonitoring, Chemosphere

Slobodník, J., Dogterom J. (2003). UNDP/GEF Danube Regional Project Strengthening the Implementation Capacities for Nutrient Reduction and Transboundary Cooperation in the Danube River Basin. Analysis of the results of the EMIS inventory and their comparison with TNMN and JDS results with particular attention to the EU Priority List of Pollutants Project Component 2.2: Development of operational tools for monitoring, laboratory and information management with particular attention to nutrients and toxic substances. Rodeco Consulting GmbH. http://www.undp-drp.org/pdf/2.2_Tools%20for%20WQMLIM%20-%20phase%201/Chapter%20III%20EMIS%20Inventory%20FINAL.pdf

Slooff W., Bremer H.J., Hesse J.M. and Matthijsen A.J.C.M. (eds.) 1991. Integrated criteria document chlorobenzenes. Report no. 710401015. RIVM.

Smeds, A., Saukko, P. (2001). Identification and quantification of polychlorinated biphenyls and some endocrine disrupting pesticides in human adipose tissue form Finland. Chemosphere 44(6): 1463-1471.

Sternbeck, J., Brorström-Lundén, E., Remberger, M., Kaj, L., Palm, A., Junedahl, E., Cato, I., 2003. WFD priority substances in sediments from Stockholm and the Svealand coastal region. Report B1538, Swedish Environmental Research Inst. (IVL), Stockholm, Sweden. http://www.ivl.se/rapporter/pdf/B1538.pdf

Susarla S, Yonezawa Y, Masunaga S. Transformation kinetics and pathways of chlorophenols and hexachlorobenzene in fresh water lake sediment under anaerobic conditions Environmental Technology 1997;18:903-911.

Thomas RS, Gustafson DL, Pott WA, Long ME, Benjamin SA, RS Yang. 1998. Evidence for hepatocarcinogenic activity of pentachlorobenzene with intralobular variation in foci incidence. Carcinogenesis 19: 1855-1862

Umegaki, K, Ikegami, S., Ichikawa, T. (1993). Effects of restricted feeding on the absorption, metabolism, and accumulation of pentachlorobenzene in rats. J. Nutr. Sci. Vitaminol. 39:11-22.

US EPA (1998). Memorandum 2/26/98 Assessment of the Dietary Cancer Risk of Hexachlorobenzene and Pentachlorobenzene as impurities in Chlorothalonil, PCNB, Picloram, and several other pesticides. DP Barcode D243499. Chemical codes 061001 (Hexachlorobenzene) & 081901 (Chlorothalonil). http://www.epa.gov/oppsrrd1/reregistration/endosulfan/hexachlorobenzene_endo.PDF

United States Environmental Protection Agency Superfund. (n.d.) APPENDIX K. Soil Organic Carbon (Koc) / Water (Kow) Partition Coefficients. http://www.epa.gov/superfund/resources/soil/appd_k.pdf

United States Environmental Protection Agency Toxics Release Inventory (TRI) Program (2007a) http://www.epa.gov/tri/tridata/index.htm#pdr. Accessed 280307.

U.S. EPA. (2007b). EPI Suite™ [computer program]. version 3.2. Washington, DC, U.S.A.: U.S. Environmental Protection Agency (EPA) Office of Pollution Prevention Toxics and Syracuse Research Company (SRC). http://www.syrres.com/esc/est_soft.htm.

US National Institute of Standards and Technology. NIST Chemistry WebBook. NIST Standard Reference Database Number 69, June 2005 Release. Available at: http://webbook.nist.gov/chemistry/

Van Gestel, C.A., W.-C. Ma and C.E. Smit. 1991. Development of QSARs in terrestrial ecotoxicology: earthworm toxicity and soil sorption of chlorophenols, chlorobenzenes and dichloroaniline. Sci. Total Environ. 109/110: 589–604.

Van de Plassche EJ, Polder MD, Canton JH (1993). Derivation of maximum persmissible concentrations for several volatile compounds for water and soil. Bilthoven, the Netherlands: National Institute of Public Health and Environmental Protection., Report no. 679101 008.

Van de Plassche, E.J., Schwegler, A.M.G.R., Rasenberg, M. and Schouten, A. (2002) Pentachlorobenzene. Dossier prepared for the third meeting of the UN-ECE Ad hoc Expert Group on POPs. Royal Haskoning report L0002.A0/R0010/EVDP/TL

Van Leeuwen, S., Traag, W., de Boer, J., 2004. Monitoring of brominated flame retardants, dioxines, PCBS and other organohalogen compounds in fish from the Netherlands. Organohalogen compounds 66: 1764-1769.

Vorkamp, K., Riget, F., Glasius, M., Pecseli, M., Lebeuf, M., Muir, D. 2004. Chlorobenzenes, chlorinated pesticides, coplanar chlorobiphenyls and other organochlorine compounds in Greenland biota. Sci Total Environ. 331: 157-175.

Vulykh N, S. Dutchak, E. Mantseva, V. Shatalov. 2005. Model assessment of potential for long-range transboundary atmospheric transport and persistence of Pentachloro-benzene. EMEP contribution to the preparatory work for the review of the CLRTAP Protocol on Persistent Organic Pollutants. EMEP MSC-E 15/2005. Meteorological Synthesizing Centre –East, Moscow, Russia.

Wang M-J, Jones KC. Behavior and fate of chlorobenzenes in spiked and sewage sludge-amended soil Environmental Science and Technology 1994;28:1843-1852.

Wang M-J, McGrath SP, Jones KC. Chlorobenzenes in field soil with a history of multiple sewage sludge applications Environmental Science and Technology 1995;29:356-362.

Wegmann, F, MacLeod, M, Scheringer, M. (2007). Pop Candidates 2007: Model results on overall persistence and Long-range transport potential using the OECD Pov & LRTP screening tool. http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/All%20chemicals%20Switzerland.pdf

WHO-IPCS International Programme on Chemical Safety. (1991). Environmental Health Criteria (EHC) 128: Chlorobenzenes other than Hexachlorobenzene. United Nations Environment Programme. International Labour Organisation. World Health Organization. Geneva. Available at: http://www.inchem.org/documents/ehc/ehc/ehc128.htm

WHO-IPCS (World Health Organization – International Programme on Chemical Safety), 1997. Hexachlorobenzene, Environmental Health Criteria 195. World Health Orgaization, Geneva, Switzerland. http://www.inchem.org/documents/ehc/ehc/ehc195.htm.

Yakata N, Sudo Y, Tadokoro H. 2006. Influence of dispersants on bioconcentration factors of seven organic compounds with different lipophilicities and structures. Chemosphere 64: 1885-1891.

Ying CO, Conolly RB, Thomas RS, Xu Y, Andersen ME, Chubb LS, Pitot HC, Yang RSH. 2001. A clonal growth model: time-course simulations of liver foci growth following penta- or hexachlorobenzene treatment in a medium-term bioassay. Cancer Research, 61: 1879-1889.

Qiao, P, Farrell, AP. (1996). Uptake of hydrophobic xenobiotics by fish in water laden with sediments from the Fraser river Environ Toxicol Chem 15: 1555-1563.