平成２１年度第１回薬事・食品衛生審議会薬事分科会
化学物質安全対策部会【第一部】
議事次第

日　時　　平成２１年７月２３日（木）　１３：３０～１４：３０

場　所　　航空会館　７階　「大ホール」

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３　報告事項
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資料　1

厚生労働省発薬食0710第103号
平成２１年７月１０日

薬事・食品衛生審議会
会長　　望月　　正隆　　殿

厚生労働大臣　　舛添　　要一

諮問書

別紙の化学物質に係る化学物質の審査及び製造等の規制に関する法律（昭和４８年法律第１１７号）に基づく措置のあり方及び同法第２７条に基づく技術上の指針の対象とすべき第二種特定化学物質含有製品の指定について、貴会の意見を求めます。

1　ペルフルオロ（オクタン－１－スルホン酸）（別名ＰＦＯＳ）又はその塩

2　ペルフルオロ（オクタン－１－スルホニル）＝フルオリド（別名ＰＦＯＳＦ）

3　ペンタクロロベンゼン

4　ｒ－１，ｃ－２，ｔ－３，ｃ－４，ｔ－５，ｔ－６－ヘキサクロロシクロヘキサン（別名α－ヘキサクロロシクロヘキサン）

5　ｒ－１，ｔ－２，ｃ－３，ｔ－４，ｃ－５，ｔ－６－ヘキサクロロシクロヘキサン（別名β－ヘキサクロロシクロヘキサン）

6　ｒ－１，ｃ－２，ｔ－３，ｃ－４，ｃ－５，ｔ－６－ヘキサクロロシクロヘキサン（別名γ－ヘキサクロロシクロヘキサン又はリンデン）

7　デカクロロペンタシクロ［５．３．０．$0^{2,6}$．$0^{3,9}$．$0^{4,8}$］デカン－５－オン（別名クロルデコン）

8　ヘキサブロモビフェニル

9　テトラブロモ（フェノキシベンゼン）（別名テトラブロモジフェニルエーテル）

１０　ペンタブロモ（フェノキシベンゼン）（別名ペンタブロモジフェニルエーテル）

１１　ヘキサブロモ（フェノキシベンゼン）（別名ヘキサブロモジフェニルエーテル）

１２　ヘプタブロモ（フェノキシベンゼン）（別名ヘプタブロモジフェニルエーテル）

別添1

ペルフルオロオクタンスルホン酸の危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 活性汚泥、底質培養物、土壌培養物中での好気的生分解試験及び下水汚泥での嫌気的生分解試験では、分解の兆候はまったく示されなかった。 【光分解性】 ・直接または間接光分解の証拠は見られなかった（EPA OPPTS ﾌﾟﾛﾄｺﾙ 835.5270）。 ・25℃における間接光分解の半減期は3.7年以上と算出された。 【加水分解性】 ・分解はまったく示されなかった（EPA OPPTS ﾌﾟﾛﾄｺﾙ 835.2210） ・半減期は41年以上とされた。 ※PFOSFは水中で速やかに加水分解されPFOSを生成する知見が別途得られている。	【BCF（経鰓的生物濃縮係数）】 ・ﾆｼﾞﾏｽ： BCF =2900（肝臓），3100（血漿） ・丸ﾊｾﾞ：BCF =約2400（全魚体） ・ﾌﾞﾙｰｷﾞﾙｻﾝﾌｨｯｼｭ：BCFk =2796 ※上記の値は、POPs条約付属書Dの基準値（BCF＜5000）以下であるが、PFOSの物性の一つである非脂肪組織中の蛋白質親和性を考慮すると、脂溶性物質を対象に設定されているBCF基準値のPFOSへの適用は不適切な可能性がある。 【BMF（経口的生物濃縮係数）】 ・ﾐﾝｸ：BMF=22（魚中の濃度から推計） ・ﾎｯｷｮｸｸﾞﾏ：BMF＞160（ﾎｯｷｮｸｱｻﾞﾗｼ中の濃度から推計） ※人為的発生源から最も遠く離れた北極圏の動物において高濃度のPFOSが検出されていることに留意。魚類・魚食性鳥類など食物連鎖上の低位種においてもPFOSが検出。また、ﾜｼなど捕食生物種は、低位にある鳥類よりも高濃度のPFOSを蓄積することが認められている。このことは、PFOSの残留性と長期蓄積性によるものである。	【反復投与毒性】 アカゲザル（強制経口90日）： 4.5mg/kg/dayで全数死亡、 0.5mg/kg/dayで消化管毒性 （カリウム塩） ラット（経口90日）：18mg/kg/dayで全数死亡、6mg/kg/dayで半数死亡、2mg/kg/dayで体重及び臓器重量変化（カリウム塩） カニクイサル（26週）：LOEL 0.03mg/kg/day 主な毒性は、胸腺萎縮（♀）、HDL、コレステロール、T3低下 ラット（混餌2年）：0.06（♂）、0.07mg/kg/day（♀）で肝細胞の病理組織的変化 【発生毒性】 ラット（二世代経口）： NOAEL:0.1mg/kg/day 0.4mg/kg/dayでF1児体重増加量低下、1.6mg/kg/dayでF1世代生存率低下、母体体重低下等（カリウム塩） ラット（♀）：妊娠17-20日目の25mg/kgで全児死亡	【慢性毒性】 ユスリカ *Chironomus tentans* ： 10dNOEC=0.0491 mg/L（成長・生存）

	・PFOS は疎水性・疎油性であるため POPs に特有な脂肪組織に蓄積するという典型的パターンに該当しない。また、PFOS は物理化学的特性が特異なため、生物蓄積のﾒｶﾆｽﾞﾑは他の POPs と異なる。		

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Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Second meeting
Geneva, 6–10 November 2006

Report of the Persistent Organic Pollutants Review Committee on the work of its second meeting

Addendum

Risk profile on perfluorooctane sulfonate

At its second meeting. the Persistent Organic Pollutants Review Committee adopted the risk profile on perfluorooctane sulfonate, on the basis of the draft contained in document UNEP/POPS/POPRC.2/11. The text of the risk profile, as amended, is provided below. It has not been formally edited.

K0653903 151206

PERFLUOROOCTANE SULFONATE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its second meeting

November 2006

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EXECUTIVE SUMMARY

1 INTRODUCTION

1.1 Chemical Identity of the proposed substance

On July 14, 2005, the government of Sweden made a proposal for listing perfluorooctane sulfonate (PFOS) and 96 PFOS-related substances in Annex A of the Stockholm Convention on Persistent Organic Pollutants (POPs).

Chemical name: Perfluorooctane Sulfonate (PFOS)

Molecular formula: $C_8F_{17}SO_3^-$

PFOS, as an anion, does not have a specific CAS number. The parent sulfonic acid has a recognised CAS number (CAS No. 1763-23-1). Some examples of its commercially important salts are listed below:

Potassium salt (CAS No. 2795-39-3)

Diethanolamine salt (CAS No. 70225-14-8)

Ammonium salt (CAS No. 29081-56-9)

Lithium salt (CAS No. 29457-72-5)

Structural formula:

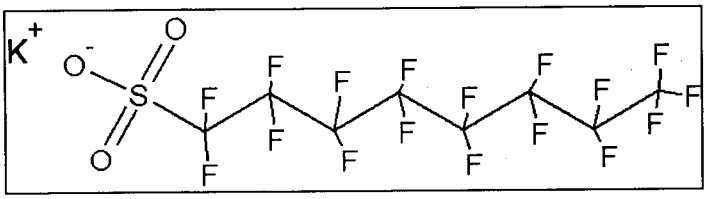

Figure 1. Structural formula of PFOS shown as its potassium salt

PFOS is a fully fluorinated anion, which is commonly used as a salt or incorporated into larger polymers. PFOS and its closely related compounds, which contain PFOS impurities or substances which can give rise to PFOS, are members of the large family of perfluoroalkyl sulfonate substances. In its regulatory measures on PFOS, the EU has addressed all molecules having the following molecular formula: $C_8F_{17}SO_2Y$, where Y = OH, metal or other salt, halide, amide and other derivatives including polymers (European Union 2006).

The physical and chemical properties of the potassium salt of PFOS are listed in Table 2.

Table 2. Physical and chemical properties of PFOS potassium salt.

(Data from OECD, 2002, unless otherwise noted).

Property	Value
Appearance at normal temperature and pressure	White powder
Molecular weight	538 g/mol
Vapour Pressure	$3{,}31 \times 10^{-4}$ Pa
Water solubility in pure water	519 mg/L (20 ± 0,5°C) 680 mg/L (24 - 25°C)
Melting point	> 400 °C
Boiling point	Not measurable
Log K_{OW}	Not measurable
Air-water partition coefficient	$< 2 \times 10^{-6}$ (3M, 2003a)
Henry's Law Constant	$3{,}09 \times 10^{-9}$ atm m^3/mol pure water

PFOS can be formed (by environmental microbial degradation or by metabolism in larger organisms) from PFOS-related substances, i.e., molecules containing the PFOS-moiety depicted in Figure 1. Although the ultimate net contribution of individual PFOS-related substances to the environmental loadings of PFOS cannot be predicted readily, there is a potential that any molecule containing the PFOS moiety could be a precursor to PFOS.

The majority of PFOS-related substances are polymers of high molecular weights in which PFOS is only a fraction of the polymer and final product (OECD, 2002). PFOS-related substances have been defined somewhat differently in different contexts and there are currently a number of lists of PFOS-related substances (Table 3). The lists contain varying numbers of PFOS-related substances that are thought to have the potential to break down to PFOS. The lists overlap to varying extents depending on the substances under consideration and the overlap between national lists of existing chemicals.

Table 3. Number of PFOS-related substances as proposed by UK – DEFRA, US – EPA, OECD, OSPAR, and Canada

Source	Number of PFOS-related substances
RPA and BRE (2004)	96
US - EPA (2002, 2006)	88[1] + 183[1]
OECD (2002)	172[1] (22 classes of perfluoroalkyl sulfonate substances)
OSPAR (2002)	48
Environment Canada (2006)	57

[1] Perfluorinated substances with different carbon chain lengths are included in the list.

A large number of substances may give rise to PFOS and thus contribute to the contamination problem. DEFRA in the United Kingdom (RPA and BRE, 2004) has recently proposed a list of 96 PFOS-related substances. However, the properties of the 96 substances have not generally been determined. According to 3M (submission to the secretariat of Stockholm Convention (SC), 2006), they may have very different environmental characteristics such as solubility, stability and ability to be absorbed or metabolised. Nevertheless, the document by the United Kingdom infers that all of these substances would give rise to the final degradation product of PFOS (RPA and BRE, 2004).

Environment Canada's ecological risk assessment defines PFOS precursors as substances containing the perfluorooctylsulfonyl ($C_8F_{17}SO_2$, $C_8F_{17}SO_3$,, or $C_8F_{17}SO_2N$) moiety that have the potential to transform or degrade to PFOS (Environment Canada, 2006). The term "precursor" applies to, but is not limited to, some 51 substances identified in the ecological assessment. However, this list is not considered exhaustive, as there may be other perfluorinated alkyl compounds that are also PFOS precursors. This information was compiled based on a survey to industry, expert judgement and CATABOL modelling, in which 256 perfluorinated alkyl compounds were examined to determine whether non-fluorinated components of each substance were expected to degrade chemically and/or biochemically and whether the final perfluorinated degradation product was predicted to be PFOS. While the assessment did not consider the additive effects of PFOS and its precursors, it is recognized that the precursors to PFOS contribute to the ultimate environmental loading of PFOS. Precursors may also play a key role in the long-range transport and subsequent degradation to PFOS in remote areas, such as the Canadian Arctic.

1.2 Conclusion of the POP Review Committee on Annex D information

The Persistent Organic Pollutants Review Committee (POPRC) evaluated Annex D information at the First meeting of the POPRC, Geneva, 7-11 November 2005, and concluded that PFOS information meets the screening criteria specified in Annex D (decision POPRC-1/7: Perfluorooctane sulfonate).

1.3 Data sources

This document on PFOS mainly builds on information that has been gathered in the hazard assessment report prepared by the UK and the USA for the OECD, and in the UK risk reduction strategy:

OECD (2002) Co-operation on Existing Chemicals - Hazard Assessment of Perfluorooctane Sulfonate and its Salts, Environment Directorate Joint Meeting of the Chemicals Committee and the Working Party on Chemicals, Pesticides and Biotechnology, Organisation for Economic Co-operation and Development, Paris, 21 November 2002.

RPA AND BRE (2004) Perfluorooctane Sulfonate – Risk reduction strategy and analysis of advantages and drawbacks, Final Report prepared for Department for Environment, Food and Rural Affairs and the Environment Agency for England and Wales.

Recent relevant information from the open scientific literature (up to May 2006) is also included. Data submitted by Parties and observers, which have been considered, are also included in this report when they add new information.

1.4 Summary of assessment and management under other programs

The hazard assessment of PFOS, prepared by the OECD in 2002, concluded that the presence and the persistence of PFOS in the environment, as well as its toxicity and bioaccumulation potential, indicate a cause of concern for the environment and human health.

An environmental risk assessment, prepared by the UK-Environment Agency, and discussed by the EU member states under the umbrella of the existing substances regulation (ESR DIR 793/93) shows that PFOS is of concern.

The final Environment Canada/Health Canada assessments of PFOS, its salts and its precursors were released in July 2006. The ecological risk assessment has concluded that PFOS and its salts are persistent and bioaccumulative, and that PFOS, its salts and its precursors have immediate or long-term harmful effects on the environment (Environment Canada, 2006).

The EU has recently decided on restrictions on the marketing and use of PFOS (European Union, 2006). The measures cover PFOS acid, its salts and PFOS derivatives, including PFOS polymers. The decision prohibits the placing on the market and use of these compounds as a substance or constituent of preparations in a concentration equal to or higher than 0,005% by mass. Furthermore, semi-finished products and articles, containing PFOS more than 0,1% by mass are prohibited. Some derogations are, however, granted in the decision. These include certain uses in photolithography processes, in photographic coatings and in metal plating, hydraulic fluids for aviation and fire fighting foams that have already been placed on the market.

The UK and Sweden have proposed the following classification for PFOS in EU (2005):

T Toxic

R40 Carcinogen category 3; limited evidence of carcinogenic effect

R48/25 Toxic; danger of serious damage to health by prolonged exposure if swallowed

R61 May cause harm to the unborn child

R51/53 Toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment has.

Norway is now considering a proposal to prohibit the use of fire fighting foams containing PFOS and PFOS-related compounds, which is the major use of these compounds today in Norway.

The Environmental Protection Agency (EPA) in the USA finalized two Significant New Use Rules (SNURs) in 2002, requiring companies to inform the EPA before manufacturing or importing 88 listed PFOS-related substances. The EPA proposed an additional SNUR under section 5(a)(2) of the Toxic Substances Control Act (TSCA) in March 2006 to include within the scope of this regulation another 183 perfluoroalkyl sulfonates with carbon chain lengths of five carbons and higher. The EPA further proposed an amendment to the Polymer Exemption rule in March 2006 which would remove from exemption polymers containing certain perfluoroalkyl moieties consisting of CF3- or longer chains, and would require that new chemical notifications be submitted on such polymers.

1.5 Status of the chemical under international conventions

OSPAR: PFOS was added to the list of Chemicals for Priority Action in June 2003.

Persistent Organic Pollutants Protocol to the Long-Range Transboundary Air Pollution Convention ("LRTAP"): The Executive Body of the UNECE LRTAP Convention agreed that PFOS be considered a POP as defined under the Protocol on POPs and requested that the UNECE Task Force on POPs continue with the review of the substance and exploring management strategies.

2 SUMMARY INFORMATION RELEVANT FOR THE RISK PROFILE

2.1 Sources

2.1.1 Production and trade

The main production process of PFOS and PFOS-related substances is electro-chemical fluorination (ECF), utilized by 3M, the major global producer of PFOS and PFOS-related substances prior to 2000.

Direct fluorination, electro-chemical fluorination (ECF):

$$C_8H_{17}SO_2Cl + 18\ HF \rightarrow C_8F_{17}SO_2F + HCl + \text{by products}$$

The reaction product, perfluorooctanesulfonyl fluoride (PFOSF)[1] is the primary intermediate for synthesis of PFOS and PFOS-related substances. The ECF method results in a mixture of isomers and homologues with about 35-40% 8-carbon straight chain PFOSF. However, the commercial PFOSF products were a mixture of approximately 70% linear and 30% branched PFOSF derivate impurities. The global production of PFOSF by 3M until the production ceased is estimated to have been 13,670 metric tonnes (1985 to 2002), with the largest yearly production volume, 3700 metric tonnes of PFOS and PFOS related substances, in 2000 (3M, Submission to SC, 2006). PFOSF may be further reacted with methyl- or ethylamine to form *N*-ethyl- and *N*-methyl perfluorooctane sulfamide and subsequently with ethylene carbonate resulting in *N*-ethyl- and -methyl-perfluorooctane sulfamidoethanol (*N*-EtFOSE and *N*-MeFOSE). *N*-EtFOSE and *N*-MeFOSE were the principal building blocks of 3M's product lines. PFOS is formed after the chemical or enzymatic hydrolysis of PFOSF (3M, 1999).

Other production methods for perfluoroalkylated substances are telomerisation and oligomerisation. However, to which extent these methods are applied for production of PFOS and PFOS-related substances is not evident.

[1] In the OECD report, 2002, perfluorooctanesulfonyl fluoride is abbreviated POSF.

On 16 May 2000, 3M announced that the company would phase-out the manufacture of PFOS and PFOS-related substances voluntarily from 2001 onwards. By the end of 2000, about 90 % of 3M's production of these substances had stopped and in the beginning of 2003 the production ceased completely.

3M´s voluntary phase-out of PFOS production has led to a reduction in the use of PFOS-related substances. This is due not only to the limited availability of these substances (3M had at the time the greatest production capacity of PFOS-related substances in the world), but also to action within the relevant industry sectors to decrease companies´ dependence on these substances.

The US Environmental Protection Agency (US EPA) compiled a list of non-US companies which are believed to supply PFOS-related substances to the global market. Of these (and excluding the plant of 3M in Belgium), six plants are located in Europe, six are located in Asia (of which four are in Japan) and one in Latin America (OECD, 2002). However, this list may not be exhaustive or current.

According to the recent submission from Japan to the secretariat of the Stockholm Convention, 2006, there is one manufacturer in Japan still producing PFOS and with a production amount of 1-10 tonnes (2005). The submission from Brazil states that lithium salt of PFOS is produced but that no quantitative data is available.

2.1.2 Uses

Perfluorinated substances with long carbon chains, including PFOS, are both lipid-repellent and water-repellent. Therefore, the PFOS-related substances are used as surface-active agents in different applications. The extreme persistence of these substances makes them suitable for high temperature applications and for applications in contact with strong acids or bases. It is the very strong carbon-fluorine binding property that causes the persistence of perfluorinated substances.

The historical use of PFOS-related substances in the following applications has been confirmed in the US and the EU.

- Fire fighting foams
- Carpets
- Leather/apparel
- Textiles/upholstery
- Paper and packaging
- Coatings and coating additives
- Industrial and household cleaning products
- Pesticides and insecticides

In the UK study (RPA and BRE, 2004), detailed information has been received from the following sectors that currently use PFOS-related substances:

- Use of existing fire fighting foam stock
- Photographic industry
- Photolithography and semiconductor
- Hydraulic fluids
- Metal plating

The sectors presented above account for the UK but are considered to be representative for EU. However, deviation in the current use pattern between EU countries cannot be excluded.

PFOS and its precursors are not manufactured in Canada but rather are imported as chemicals or products for Canadian uses. They may also be components in imported manufactured articles. It is estimated that the majority of PFOS has been used as water, oil, soil and grease repellents (e.g. on fabric, leather, paper, packaging, rugs and carpets) and as surfactants (e.g. in fire fighting foams and coating additives) (Environment Canada, 2006).

PFOS and its precursors are not manufactured in the US, but can be imported either as chemicals or in products for the specific limited uses that were excluded from regulation. These comprise use as an anti-erosion additive in aviation hydraulic fluids; use as a component of a photoresist substance, including a photo acid generator or surfactant, or as a component of an anti-reflective coating, used in a photomicrolithography process to produce semiconductors or similar components of electronic or other miniaturized devices; use in coatings for surface tension, static discharge, and adhesion control for analog and digital imaging films, papers, and printing plates, or as a surfactant in mixtures used to process imaging films; and use as an intermediate only to produce other chemical substances to be used solely for these uses. Historically, PFOS and its precursors were also used as surfactants in fire fighting foams and in industrial and household cleaning products; in carpet, textile, leather, and paper coatings; and in termite and ant bait insecticide products. Stocks of PFOS and PFOS-containing products that were in existence at the time the US regulations were promulgated in 2002 could continue to be used in any application until they were consumed without violating the regulation, except that the PFOS-related insecticide products are subject to a phase-out agreement prohibiting their use after 2015.

The table below outlines the estimated current demand for PFOS-related substances in these applications in the EU (RPA and BRE, 2004).

Estimated Current (2004) Demand for PFOS Related Substances in the EU	
Industry Sector	Quantity (kg/year)
Photographic industry	1,000
Photolithographic and semi-conductors	470
Hydraulic fluids	730
Metal plating	10,000

In the survey on production and use of PFOS and related substances performed by OECD in 2004 (published 2005), data concerning PFOS were difficult to separate from data on other perfluoroalkyl sulfonates.

Fire Fighting Foams

The fire fighting foams can be grouped in two main categories:

- Fluorine-containing foam types (some of them consist of PFOS-related substances)
- Fluorine-free foam types

Since the announcement of the voluntary cessation of production of PFOS-related substances by 3M, the presence of PFOS in fire fighting foams has gradually decreased (RPA and BRE, 2004).

Historically, in Canada, the most significant imports of PFOS, itself, were in the form of the potassium salt, used for fire-fighting foams (Environment Canada, 2006). Canada has also identified that existing stocks of PFOS-containing fire fighting foams could be a continued significant source of releases.

An industry survey conducted in the US by the Fire Fighting Foam Coalition in 2004 reported that the total inventory of aqueous film-forming foam in the US was approximately 9.9 million gallons, of which about 45% was PFOS-based stocks produced before 2003, with the other 55% comprised of telomer-based foams.

Textile, Carpet and Leather Protection

PFOS-related substances have been used to provide soil, oil and water resistance to textiles, apparels, home furnishings and upholstery, carpets, and leather products. Since 3M's withdrawal from the market, PFOS-related substances are used to a much smaller extent for these applications (RPA AND BRE, 2004).

Paper and Packaging Protection

PFOS-related substances have been used in the packaging and paper industries in both food packaging and commercial applications to impart grease, oil and water resistance to paper, paperboard and packaging substrates. According to 3M, fluorochemicals were used for both food contact applications (plates, food containers, bags and wraps) and non-food applications (folding cartons, containers and carbonless forms and masking papers). Since 3M's withdrawal from the market, PFOS related substances are used to a much smaller extent for these applications (RPA and BRE, 2004).

Coatings and Coating Additives

3M indicates that prior to its voluntary phase-out of PFOS production, the company would sell fluorochemical polymer coatings and coating additives which were used undiluted or diluted with water or butyl acetate to impart soil or water repellence to surfaces (including printing circuit boards and photographic film) (RPA and BRE, 2004).These polymers contained fluorocarbon residuals at a concentration of 4% or less. Other applications for aqueous coatings are to protect tile, marble and concrete. It is unclear which of these products were actually based on PFOS-related substances.

A survey in the UK among members of the British Coatings Federation (BCF) showed that the use of PFOS-related substances for these purposes is very limited (RPA and BRE, 2004).

Industrial and Household Cleaning Products (Surfactants)

3M PFOS-based products were sold in the past to a variety of formulators to improve the wetting of water-based products marketed as alkaline cleaners, floor polishes (to improve wetting and levelling), denture cleansers and shampoos. Several of these products (alkaline cleaners, floor polishes, shampoos) were marketed to consumers; some products were also sold to janitorial and commercial services. A number of the alkaline cleaners were spray-applied.

With regard to the UK cleaning products industry, the responses received do not indicate the use of PFOS-related substances in industrial and household cleaning products. Based on information provided in product registers, the Swedish National Chemicals Inspectorate (KemI) has indicated that PFOS-related substances are still being used in Sweden for both industrial and household use (RPA and BRE, 2004).

Photographic Industry

PFOS-based chemicals are used for the following purposes in mixtures, in coatings applied to photographic films, papers, and printing plates (RPA and BRE, 2004):

- Surfactants
- Electrostatic charge control agents;

- Friction control agents;
- Dirt repellent agents; and
- Adhesion control agents

Photolithography and Semiconductors

Photoresist

Semiconductor manufacturing comprises up to 500 steps, of which there are four fundamental physical processes:

- Implant
- Deposition
- Etch
- Photolithography

Photolithography is the most important step towards the successful implementation of each of the other steps and, indeed, the overall process. It shapes and isolates the junctions and transistors; it defines the metallic interconnects; it delineates the electrical paths that form the transistors; and joins them together. Photolithography reportedly represents 150 of the total of 500 steps mentioned above. Photolithography is also integral to the miniaturization of semiconductors (RPA and BRE, 2004).

PFOS is used as a photoacid generator (PAG) in a mechanism called chemical amplification that increases the sensitivity of photoresist to allow etching images smaller than wavelength of light.

Antireflective Coatings

A number of resist suppliers sell antireflective coatings (ARC), subdivided into Top (TARC) and Bottom (BARC) coatings and used in combination with deep ultra violet (DUV) photoresist. The process involves placing a thin, top coating on the resist to reduce reflective light, in much the same way and for the same purposes that eyeglasses and camera lenses are coated.

Hydraulic Fluids for the Aviation Industry

Hydraulic fluids were initially used in aircraft to apply brake pressure. As larger and faster aircraft were designed, greater use of hydraulic fluids became necessary. An increase in the number of hydraulic fluid fires in the 1940s necessitated work towards developing fire resistant fluids. The first of these fluids was developed around 1948, when fire resistant hydraulic fluids based on phosphate ester chemistry were developed.

Perfluorinated anions act by altering the electrical potential at the metal surface, thereby preventing the electrochemical oxidation of the metal surface under high fluid flow conditions (RPA and BRE, 2004). As a result, hydraulic fluids based on phosphate ester technology and incorporating additives based on perfluorinated anions are used in all commercial aircraft, and in many military and general aviation aircraft throughout the world, as well as by every airframe manufacturer (RPA and BRE, 2004).

Metal Plating

The main uses of PFOS-related substances in metal plating are for chromium plating, and anodising and acid pickling. PFOS related substances lower the surface tension of the plating solution so that mist containing chromic acid from the plating activity is trapped in solution and is not released to air (RPA and BRE, 2004).

Other

There is information on other historical or current PFOS applications such as in pesticides, medical applications, mining and oil surfactants, flame retardants and in adhesives. Based on current understanding, these applications represent a minor part of known PFOS applications and are therefore not further elaborated in this profile.

2.1.3 Releases to the environment

There is to date very limited information regarding the emissions and pathways of PFOS to the environment. The occurrence of PFOS in the environment is a result of anthropogenic manufacturing and use, since PFOS is not a naturally occurring substance.

Releases of PFOS and its related substances are likely to occur during their whole life cycle. They can be released at their production, at their assembly into a commercial product, during the distribution and industrial or consumer use as well as from landfills and sewage treatment plants after the use of the products (3M, 2000).

Manufacturing processes constitute a major source of PFOS to the local environment. During these processes, volatile PFOS-related substances may be released to the atmosphere. PFOS and PFOS-related substances could also be released via sewage effluents (3M, 2000). High local emissions are indicated by one study that showed extremely high concentrations of PFOS in wood mice collected in the immediate vicinity to 3M's fluorochemical plant in Antwerpen, Belgium (Hoff et al., 2004). High concentrations of PFOS were also found in liver and blood from fish collected in the Mississippi River at the immediate vicinity of another 3M fluorochemical plant at Cottage Grove in Minnesota (MPCA, 2006).

Fire training areas have also been revealed to constitute a source of PFOS emissions due to the presence of PFOS in fire-fighting foams. High levels of PFOS have been detected in neighbouring wetlands of such an area in Sweden (Swedish EPA, 2004) as well as in groundwater in the US close to a fire-training area (Moody et al., 2003).

An investigation on the uses of PFOS and PFOS-related compounds in Norway in 2005 shows that approximately 90% of the total use is in fire extinguishers (Submission to SC, 2006). Estimated releases of PFOS related to fire extinguishers are at least 57 tonnes since 1980 to 2003 (2002; 13-15 tonnes). Remaining quantities of fire extinguisher foam in Norway are estimated to be a minimum of 1.4 million litres, which corresponds to an amount of approximately 22 tonnes PFOS. Releases from the municipal sector in Norway, 2002, were estimated to be 5-7 tonnes (Submission to SC, 2006).

The use of PFOS in semiconductors is estimated to result in a release of 43 kg per year in the EU, according to the Semiconductur Industry Association (SIA) (SIA, Submission to SC, 2006). This corresponds to 12 % of the total PFOS use in this application. PFOS released in the USA from semiconductors is estimated to be in the same range (SIA, 2006).

The releases of sulfonated perfluorochemicals, including PFOS or PFOS-related substances, from different product usages have been estimated (3M Speciality Materials, 2002). For example, garments treated with home-applied products, are expected to lose 73 % of the treatment during cleaning over a 2-year life span. A loss of 34 % to air is expected from spray can products during use, while up to 12.5 % of the original content may be remaining in the cans at the time of disposal.

One route for PFOS and PFOS-related substances to the environment may be through sewage treatment plants (STPs) and landfills, where elevated concentrations have been observed compared to background concentrations. Once released from STPs, PFOS will partially adsorb to sediment and organic matter. A substantial amount of PFOS may also end up in agricultural soil, due to the

application of sewage sludge. The primary compartments for PFOS are therefore believed to be water, sediment and soil (RIKZ, 2002).

Dispersion of PFOS in the environment is thought to occur through transport in surface water, or oceanic currents (Yamashita *et al.*, 2005, Caliebe *et al.*, 2004), transport in air (volatile PFOS-related substances), adsorption to particles (in water, sediment or air) and through living organisms (3M, 2003a).

One major obstacle when trying to estimate the releases of PFOS to the environment is that PFOS can be formed through degradation of PFOS-related substances. The rate and the extent of that formation are presently unknown. In a study on Swedish STPs, higher concentrations of PFOS were found in the effluents compared to incoming sewage water, which could indicate that PFOS was formed from PFOS-related substances (Posner and Järnberg, 2004).

2.2 Environmental fate

2.2.1 Persistence

PFOS is extremely persistent. It does not hydrolyse, photolyse or biodegrade in any environmental condition tested (OECD, 2002).

A study on the hydrolysis of PFOS in water has been performed following US-EPA OPPTS protocol 835.2210. The study was conducted at pH varying from 1.5 – 11.0 and at a temperature of 50°C, to facilitate hydrolysis, but did not indicate any degradation of PFOS. The half-life of PFOS was set to be greater than 41 years.

A study on the photolysis of PFOS in water following US-EPA OPPTS protocol 835.5270 has been conducted. No evidence of direct or indirect photolysis was observed under any of the conditions tested. The indirect photolytic half-life of PFOS at 25°C was calculated to be more than 3.7 years.

Biodegradation of PFOS has been evaluated in a variety of tests. Aerobic biodegradation of PFOS has been tested in activated sewage sludge, sediment cultures and soil cultures in several studies. Anaerobic biodegradation has been tested in sewage sludge. None of the studies demonstrated any signs of biodegradation.

Modelling with a simulator program of microbial degradation, the CATABOL system, and expert judgment predicted that of 171 studied perfluorinated substances over 99% would biodegrade to extremely persistent perfluorinated acids. Of them, 109 substances were predicted to end up as perfluorinated sulfonic acids, including PFOS, and 61 as perfluorinated carboxylic acids (Dimitrov et al., 2004).

The only known condition whereby PFOS is degraded is through high temperature incineration under correct operating conditions (3M, 2003a). Potential degradation at low temperature incineration is unknown.

2.2.2 Bioaccumulation

It should be noted that PFOS does not follow the "classical" pattern of partitioning into fatty tissues followed by accumulation, which is typical of many persistent organic pollutants. This is because PFOS is both hydrophobic and lipophobic. Instead, PFOS binds preferentially to proteins in the plasma, such as albumin and β-lipoproteins (Kerstner-Wood et al., 2003), and in the liver, such as liver fatty acid binding protein (L-FABP; Luebker et al., 2002). Because of the unusual physical-chemical characteristics of PFOS, the mechanism of bioaccumulation probably differs from other POPs.

In a study following OECD protocol 305, the bioaccumulation of PFOS in bluegill sunfish (*Lepomis macrochirus*) has been tested. The whole-fish kinetic bioconcentration factor (BCFK) was determined to be 2796 (3M, 2002).

In another study on rainbow trout (*Oncorhynchus mykiss*), a bioconcentration factor (BCF) in liver and plasma was estimated to be 2900 and 3100, respectively (Martin, *et al.*, 2003).

When strictly looking at the BCF values, it is clear that these values are below the numeric BCF criteria in Stockholm Convention Annex D (the reported BCF values are below 5000) but, in this particular case, as noted above, the BCF numeric criteria may not adequately represent the bioaccumulation potential of the substance. Monitoring data from top predators at various locations show highly elevated levels of PFOS and demonstrate substantial bioaccumulation and biomagnification (BMF) properties of PFOS. It is notable that the concentrations of PFOS found in livers of Arctic polar bears exceed the concentrations of all other known individual organohalogens (Martin et al., 2004a). Based on the concentration of PFOS in predators (e.g., the polar bear) in relation to the concentration in their principal food (e.g., seals), hypothetical BMF values can be calculated. Such data are reported in Table 4. It should be noted that there are uncertainties in these comparisons. Even if either liver or blood concentrations are compared in two species, species differences in specific protein binding in that particular compartment may affect the concentration in the organ without having affected the whole-body concentration of the substance.

Table 4. Measured concentrations of PFOS in biota from various locations. Calculated BMF is shown where applicable.

Species and Location	Concentrations of PFOS	Reference
• Polar Bear, Canadian Arctic	- Concentrations of PFOS in liver (1700 – > 4000 ng/g) exceeding all other individual organohalogens. - BMF > 160 based on concentrations in Arctic seals.	Martin et al., 2004a.
• Arctic fox, Canadian Arctic	- Very high concentrations of PFOS in liver (6.1 - 1400 ng/g)	Martin et al., 2004a.
• Mink, US	- Very high concentrations of PFOS in liver (40 - 4870 ng/g). - BMF = 22 based on data from fish in the same area. - nother mink study also show very high concentrations of PFOS in liver (1280 - 59 500 ng/g, mean 18 000 ng/g,) - BMF ~145 to ~4000 based on data from their prey such as crayfish (whole body), carp (muscle) and turtles (liver	Giesy and Kannan, 2001 Kannan et al., 2005

• Bald Eagle, US	- Very high concentrations of PFOS in plasma (1 – 2570 ng/g).	Giesy and Kannan 2001.
• Dolphin, US	- Very high concentrations of PFOS in liver (10 – 1520 ng/g).	3M, 2003a.
• Seal in the Bothnian Sea, Finland	- Very high concentrations of PFOS in liver (130 – 1100 ng/g). - BMF > 60 based on data from salmon in the same area.	Kannan et al., 2002

In a study by Kannan et al. (2005), the whole body BCF for round gobies (*Neogobius melanostomus)* was calculated to be approximately 2400, which is comparable with laboratory data. PFOS concentrations in fish (whole body of round gobies) compared to concentrations in liver of salmon results in BMFs of approximately 10-20. In bald eagles, the mean PFOS concentration in the livers, 400 ng/g ww, gives a BMF of four to five when compared to fish at higher trophic levels in the study. For mink, BMFs from 145 to 4000 can be calculated when based on the mean liver concentration, 18 000 ng/g ww, compared to their prey items such as crayfish (whole body), carp (muscles) and turtles (liver).

In general, data show that animals at higher trophic levels have higher concentrations of PFOS than animals at lower trophic levels, indicating that biomagnification is taking place. For instance, a trophic magnification factor (TMF) of 5,9 was calculated for PFOS based on a pelagic food web including: one invertebrate species, Mysis; two forage fish species, rainbow smelt and alewife; and a top predator fish species, lake trout. A diet-weighted bioaccumulation factor of approximately 3 was determined for the trout (Martin et al., (2004b).

Morikawa *et al.* (2005) showed a high bioaccumulation in turtles. Results from a study performed by Tomy *et al.* (2004a) indicated that PFOS biomagnified in an eastern Arctic marine food web (liver concentrations of PFOS were used for seabirds and marine mammals). Houde *et al.* (2006) showed PFOS biomagnification in the Atlantic Ocean bottlenose dolphin food web.

A study by Bossi *et al.* (2005a) further supports that biomagnification is taking place. In this study, a preliminary screening of PFOS and related compounds has been performed in liver samples of fish, birds and marine mammals from Greenland and the Faroe Islands. PFOS was the predominant fluorochemical in the biota analyzed, followed by perfluorooctane sulfonamide (PFOSA). The results from Greenland showed a biomagnification of PFOS along the marine food chain (shorthorn sculpin < ringed seal < polar bear).

It is assumed that the main and most relevant route of exposure to PFOS for birds is through the diet as biomagnification in bird tissues can occur this way. BMFs above one are reported for several bird species collected in the Gulf of Gdansk (Gulkowska *et. al.* 2005). Kannan *et al.* (2005) reported a BMF of 10 to 20 in bald eagles (relative to prey items). Tomy *et al.* (2004a) calculated a trophic level BMF for black-legged kittiwake:cod of 5.1 and a BMF for glaucous gull:cod of 9.0. Newsted *et al.* (2005) indicated that PFOS has relatively shorter half-lives in blood and liver tissue in birds compared to mammals. For example, the estimated elimination half-life for PFOS from serum is 13.6 days in male mallards whereas in male rats, it is greater than 90 days. A recent study has suggested that PFOS is excreted relatively rapidly from birds (Kannan *et al.*, 2005). However, if birds are chronically exposed to PFOS in their diet, biomagnification can still occur. Environmental monitoring of birds in northern parts of their range in fact indicates accumulation of PFOS.

The fact that PFOS binds to proteins leads to the relevant question -- *at what concentrations of PFOS will the binding sites on these proteins be saturated?* Serum albumin is most likely the binding pool of PFOS (Jones *et al.*, 2003) and several studies have been carried out with regard to bioconcentration in plasma. In Ankley *et al.* (2005), the bioconcentration in fish was studied at concentrations of PFOS in water up to 1 mg /L; the concentration of PFOS in water and plasma followed an almost linear relationship in the doses tested up to 0.3 mg/l without any signs of saturation (1 mg/l was not tested due to mortality at that dose). This is far above environmentally relevant concentrations.

In a study by 3M (2003a), the bioconcentration factor (BCF) in whole fish was determined to be approximately 2800 at a PFOS concentration of 86 µg/l, based on calculations of uptake and depuration of PFOS. Steady-state levels were attained after 49 days of exposure. Depuration occurred slowly and 50% clearance for whole fish tissues was estimated to be 152 days. Due to mortality, a BCF could not be calculated for the other concentration used, 870 µg/l. Thus, it is not likely that saturation of serum protein binding sites will limit the bioconcentration of PFOS in fish. In Cynomolgus monkeys, cumulative doses of PFOS (0,03, 0,15, or 0,75 mg/kg/day, orally, for 182 days) showed a linear increase in plasma at the low- and mid-dose groups while a nonlinear response was showed in the high-dose group (Covance Laboratories, Inc. 2002a). We are not aware of similar data in other mammals, but considering the high level of bioaccumulation observed in mammals, and that mammalian serum contains high concentrations of protein, binding sites are not likely to limit the bioaccumulation of PFOS in environmentally exposed mammals.

2.2.3 Long-range environmental transport

The potassium salt of PFOS has a measured vapour pressure of 3.31×10^{-4} Pa (OECD, 2002). Due to this vapour pressure and a low air-water partition coefficient ($< 2 \times 10^{-6}$), PFOS itself is not expected to volatilise significantly. It is therefore assumed to be transported in the atmosphere predominantly bound to particles, because of its surface-active properties, rather than in a gaseous state.

Some of the PFOS-related substances have a considerably higher vapour pressure than PFOS itself, and are as a result more likely to be volatile. The vapour pressures of precursors, such as N-EtFOSEA and N-MeFOSEA, may exceed 0.5 Pa (1000 times greater than that of PFOS) (Giesy and Kannan 2002). Other PFOS precursors considered volatile include N-EtFOSE alcohol, N-MeFOSE alcohol, N-MeFOSA and N-EtFOSA (3M, 2000). These precursors to PFOS could evaporate into the atmosphere and be more widely transported through air than is possible for PFOS itself. Once in the atmosphere, they can remain in gas phase, condense on particles present in the atmosphere and be carried or settle out with them, or be washed out with rain (3M, 2000). Martin *et al.* (2002) measured the air in Toronto and Long Point, Ontario, for some precursors of PFOS. They found an average N-MeFOSE alcohol concentration of 101 pg/m^3 in Toronto and 35 pg/m^3 at Long Point. The average concentrations of N-EtFOSE alcohol were 205 pg/m^3 in Toronto and 76 pg/m^3 in Long Point.

For precursors released to water, the vapour pressure may be significant enough to allow the substance to enter into the atmosphere. For N-EtFOSE alcohol, the tendency to leave the water phase is indicated by its relatively high Henry's law constant (1.9×10^3 Pa·m^3·mol^{-1}) (Hekster *et al.* 2002). It has been reported that when these PFOS precursors are present as residuals in products, they could evaporate into the atmosphere when the products containing them are sprayed and dried (3M, 2000).

PFOS has been detected in rainwater from an urban center in Canada with a concentration of 0.59 ng/L. Whether or not PFOS originates from precursors either being transported and subsequently wet deposited and degraded to PFOS, or atmospherically degraded and then wet deposited, is unclear. Measurements of potential precursors for PFOS were not performed in this study (Loewen *et al*, 2005)

The atmospheric half-life of PFOS is expected to be greater than two days. This statement, while not specifically tested, is based on the fact that PFOS has exhibited extreme resistance to degradation in all tests performed. However, an atmospheric half-life of 114 days has been calculated for PFOS using an AOP computer modeling program v1.91 (Environment Agency,, 2004). The indirect photolytic half-life of PFOS at 25°C has been estimated to be more than 3.7 years (OECD, 2002).

How perfluoralkyl acid substances have come to be globally disseminated in the environment has been the key question, since, for example, the vapour pressure and Henry's law constant of PFOS indicates it is too involatile and therefore unlikely to enter directly into the atmosphere (Stock *et al.* 2004). Therefore it has been hypothesized that PFOS must be globally distributed via more volatile, neutral airborne contaminants that undergo long-range transport and then degrade to yield the free acids.

In support, Stock *et al.* (2004) have recently reported that polyfluorinated sulfonamides are widely distributed throughout the North American troposphere. Mean concentrations ranged from 22-403 pg/m^3 with the dominant polyfluorinated contaminant dependent on the sampling location.

High mean concentrations of N-methyl perfluorooctane sulfonamidoethanol (NMeFOSE) of 359 pg/m^3, were identified in the air of Griffin, Georgia. The authors speculate that, as Griffin is located in the midst of the main carpet manufacturing and treatment zone of the US, it probably is entering the environment from carpet treatment products, many of which consist of fluorinated molecules linked to polymeric materials. For example, it is possible that free chemical may be left in the carpet fibres, with publicly available information on 3M produced products indicating the concentration of free polyfluorinated sulfonamides is typically 1-2% or less. Alternatively, it is postulated that chemically bound NMeFOSE may also be released from carpets due to chemical, physical, and/or biological degradation processes.

Support for this hypothesis comes from Shoeib *et al.* (2004), who measured both NMeFOSE and the related N-ethyl perfluorooctane sulfonamidoethanol (NEtFOSE) in both indoor and outdoor air. Mean indoor air concentrations for these were 2590 and 770 pg/m^3, respectively, and the ratios between indoor and outdoor air were 110 and 85, respectively. Again carpets were identified as a possible source of NMeFOSE, and high usage of paper in the building as a possible source of NEtFOSE. Paper products were also suggested by Stock *et al.* (2004) as a possible source for the high levels of NEtFOSE in the air of Reno, Nevada.

Recently Dinglasan-Panlilio and Maybury (2006) have demonstrated that residual fluorinated substances detected in materials, including 0.39% of a perfluoroalkyl sulfonamido alcohol present in a commercially available carpet protector product, are the likely sources for these volatile precursors. Further N-methyl perfluorobutane sulfonamidoethanol (NMeFBSE) has been demonstrated in the laboratory to degrade to perfluorobutane sulfonate (PFBS), albeit in low yield (D'eon et al, 2006).

PFOS has been measured in a wide range of biota in the Northern Hemisphere such as the Canadian Arctic, Sweden, the US and the Netherlands. In a study by Martin *et al.* (2004a), the levels of PFOS were measured in liver samples from biota in the Canadian Arctic and were found in the vast majority of the species examined. The presence of PFOS in Arctic biota, far from anthropogenic sources, demonstrates the potential of PFOS for long-range transport. The mechanisms of this transport are not known, but it could be due to the transport of volatile PFOS-related substances that eventually degrade to PFOS.

While precursors will undergo degradation once released to the environment, transformation rates may vary widely. Precursors that reach a remote region through the atmosphere or other media may be subject to both abiotic and biotic degradation routes to PFOS (Giesy and Kannan 2002a; Hekster *et al.* 2002). The mechanisms of this degradation are not well understood. When rats metabolize N-MeFOSE-based compounds, several metabolites have been confirmed in tissue samples, including PFOS and N-MeFOSE alcohol (3M Environmental Laboratory 2001a, 2001b). PFOS appears to be the final product of rat and probably other vertebrate metabolism of POSF-based substances.

A recent study performed with rainbow trout (*Onchorhynchus mykiss)* liver microsomes has demonstrated that *N*-ethyl perfluorooctanesulfonamide (N-EtPFOSA) is a precursor of PFOS in fish (Tomy et al., 2004b). These findings combined with the recent measurements of concentrations up to 92.8 ± 41.9 ng/g wet weight of *N*-EtPFOSA in aquatic organisms from Arctic regions (Tomy et al., 2004a) strengthen the hypothesis that perfluorinated sulfonamides are one of the volatile precursors of PFOS transported over long distances to the Arctic. However, the hypothesis that these volatile precursors reach the Arctic latitudes by atmospheric transport has not yet been confirmed by atmospheric measurements (Bossi et al., 2005b)

2.3 Exposure

2.3.1 Measured environmental levels

A screening study was assigned by the Swedish Environmental Protection Agency (Swedish EPA) and performed by ITM, Institute of Applied Environmental Research, on the levels of PFOS in the Swedish environment (Swedish EPA, 2004). The results showed highly elevated levels of PFOS in a wetland in the vicinity of a fire drill area with a declining gradient out in the adjacent bay (2.2 – 0.2µg/L). Elevated levels were also detected outside sewage treatment plants (STPs) and landfills. Effluents from STPs contained levels of PFOS up to 0.020 µg/L and leachate levels from landfills were between 0.038 – 0.152 µg/L.

The occurrence of PFOS and other perfluoroalkyl sulfonate substances in open ocean waters such as the Atlantic and the Pacific Ocean have been investigated. The detection of PFOS in oceanic waters suggests another potential long-range transport mechanism to remote locations such as the Arctic. The results showed that PFOS is present in central to western Pacific Ocean regions in concentrations ranging from 15 – 56 pg/L, comparable to the concentrations in the mid-Atlantic ocean. These values appear to be the background values for remote marine waters far from local sources (Taniyasu *et al.*, 2004). PFOS was also detected in oceanic waters in several coastal seawaters from Asian countries (Japan, China, and Korea) at concentrations ranging from 1.1 - 57 700 $pg.L^{-1}$ (Jin *et al.*, 2004; Yamashita *et al.*, 2005). PFOS was also observed in the North Sea (estuary of the river Elbe, German Bight, southern and eastern North Sea) (Caliebe *et al.*, 2004).

In a study in cities across China, PFOS was detected in all water samples (surface and sea water, groundwater, municipal and industrial effluents and tap water), showing that PFOS pollution existed generally in water compartments in China. Concentrations were generally at levels of approximately 1 ngéL (Jin *et al.*, 2004).

Studies in the US have identified the presence of PFOS in surface water and sediment downstream of a production facility, as well as in wastewater treatment plant effluent, sewage sludge and landfill leachate at a number of urban centres in the US (3M Multi City study, reviewed in OECD (2002) and 3M (2003a). Four of the cities (Decatur (AL), Mobile, Columbus (GA), Pensacola) were cities that have manufacturing or industrial use of fluorochemicals; two of the cities (Cleveland (TN), Port St. Lucie) were control cities that do not have significant fluorochemical activities. The ranges of PFOS levels in these cities are provided in Table 5.

Table 5. Environmental Levels of PFOS in Six US Urban Centres in the US (from OECD, 2002)

Medium	Range of PFOS levels (µg/L or µg/kg)
Municipal wastewater treatment plant effluent	0.041 - 5.29
Municipal wastewater treatment plant sludge	0.2 - 3.120 (dry weight)
Drinking water	ND - 0.063
Sediment	ND - 53.1 (dry weight)
Surface water	ND - 0.138
'Quiet' water	ND - 2.93

Note: ND: not detected

The control cities' samples generally inhabited the lower end of the above ranges, except for the municipal wastewater treatment plant effluent and sludge findings for one of the control cities (Cleveland), which were intermediate in their ranges, and the 'quiet' water samples at control city (Port St. Lucie), which were the highest. In Canada, suspended sediment samples were collected annually at Niagara-on-the-Lake in the Niagara River over a 22 year period (1980-2002). PFOS concentrations ranged from 5 to 1100 $pg.g^{-1}$ (Furdui *et al.*, 2005). Preliminary findings suggest that PFOS concentrations increased during the study period from < 400 $pg.g^{-1}$ in the early 1980s to > 1000 $pg.g^{-1}$ in 2002.

Samples of effluent from fifteen representative industry sectors have been analysed for PFOS (Hohenblum *et al*, 2003). The industry sectors were printing (1 site), electronics (3), leather, metals, paper (6), photographic and textiles (2). The PFOS levels ranged from 0-2.5 µg/L (2.5 µg/L for leather, 0.120 µg/l for metal, 0.140-1.2 µg/l at four paper sites, 1.2 µg/l for photographic, not found in textiles or electronics).

Groundwater from below an air force base in Michigan, US, has been sampled (Moody et al, 2003). Fire fighting foams containing PFOS had been used there in training exercises from the 1950s to 1993 when the base was decommissioned. The groundwater was found to contain PFOS, at levels from 4 - 110 µg/l.

Sixteen Great Lakes water samples (eight locations) were analysed for perfluorooctane surfactants. PFOS was present in all samples with a concentration range of 21-70 ng/L. Three PFOS precursors were also found in the water samples. N-EtFOSAA (4.2-11 ng/L) and PFOSA (0.6 -1.3 ng/L) were present in nearly all samples while PFOSulfinate was identified at six out of eight locations (2.2-17 ng/L) (Boulanger et al, 2004). PFOS was detected in surface water as a result of a spill of fire-fighting foam from the Toronto International Airport into nearby Etobicoke Creek. Concentrations

of PFOS ranging from <0.017 to 2210 $\mu g.L^{-1}$ were detected in creek water samples over a 153-day sampling period. PFOS was not detected at the upstream sample site (Moody *et al.* 2003).

PFOS and related fluorochemicals have been detected in animals in a number of studies in a variety of locations around the globe. Generally, the highest concentrations are found in top predators in food chains containing fish. The highest North American or circumpolar concentration of PFOS in mammal tissue reported in the published literature is 59 500 $\mu g.kg^{-1}$ ww in mink liver from USA (Kannan *et al.*, 2005a).

Martin *et al.* (2004a) measured the levels of PFOS in liver samples from biota in the Canadian Arctic. PFOS was found in the vast majority of the samples and higher levels were found in animals at the top of the food chain. The highest levels were found in polar bear, with a mean level of 3100 ng/g from seven animals (maximum value > 4000 ng/g). The concentrations of PFOS in polar bear are 5-10 times higher than the concentration of all other perfluoroalkyl substances and were higher than any other previously reported concentrations of persistent organochlorine chemicals (e.g., PCBs, chlordane or hexachlorocyclohexane) in polar bear fat (Martin *et al.*, 2004a). PFOSA, a precursor to PFOS, was also found in most of the samples. The concentration of PFOSA was higher than that of PFOS in fish, but not in mammals. This could indicate that PFOSA has been metabolised to PFOS in mammals and the high concentrations may be the result of both direct exposure to PFOS and metabolism from PFOSA.

PFOS is found in birds worldwide. In North America, PFOS has been found in eagles in the Great Lakes, mallards in the Niagara River, loons in northern Quebec, gulls in the Arctic and in Canadian migratory species in the United States (e.g., common loon in North Carolina). In Canadian or Canada-US migratory species, concentrations have been measured in liver ranging from not detectable to 1780 ng/g for loon in northern Quebec and bald eagle in Michigan, in blood plasma ranging from <1- 2220 ng/g blood plasma in bald eagles, and in eggs and egg yolk ranging from 21-220 ng/g in double-crested cormorant in Manitoba. In several monitoring studies, piscivorous water birds were found to have some of the highest liver and serum PFOS concentrations compared to other species (Newsted *et al.*, 2005). In a study of birds in the Niagara River Region, piscivorous birds (common merganser, bufflehead) contained significantly greater PFOS concentrations than non-piscivorous birds (Sinclair *et al.*, 2006). Preliminary data on temporal trends show an increase in bird PFOS concentrations, in two Canadian Arctic species (thick-billed murres and northern fulmars) from 1993 to 2004 (Butt *et al.*, 2005). It is noted that concentrations of PFOS in plasma have been reported in eagle, gulls and cormorants around the Great Lakes and in the Norwegian Arctic ranging from <1 ng/g to 2220 ng/g .

Kannan and Giesy (2002b) have summarised results of analyses on archived tissue samples. The tissues analysed came from marine mammals, birds, fish, reptiles and amphibians from around the world, including the Arctic and Antarctic Oceans. Samples collected in the 1990s were used. Around 1700 samples were analysed, with concentrations in liver, egg yolk, muscle or blood plasma determined. The detection limit varied from 1 ng/g to 35 ng/g wet weight. A summary of the results is shown in Table 6.

Table 6. Maximum concentrations of PFOS in various species as well as frequency of detection. Based on Kannan and Giesy (2002a)

Species	Maximum concentration ng/g wwt.	Frequency of detection
Marine mammals	1520	77%
Mink and otter	4900	100%
Birds	2570	60%
Fish	1000	38%

PFOS was detectable in most of the samples, including those from remote marine locations, at concentrations >1 ng/g. The authors compared the results from remote areas with those from more industrial locations and noted that PFOS is widely distributed in remote regions, including the Polar Regions, but that the levels found in more urban and industrial areas (e.g. the Baltic, Great Lakes) are several times higher. The tissues of fish-eating birds in Canada, Italy, Japan and Korea all contained detectable levels of PFOS, suggesting that they are exposed through the fish they consume. A summary of several studies is given in Table 7.

Table 7. Monitored levels of PFOS in animals (data from selected studies, based on OECD, 2002)

Description	Reference	Reported Highest Concentrations (Max; Mean)	Location
Global monitoring survey of marine mammals (Florida, California, Alaska, northern Baltic Sea, Mediterranean Sea, Arctic, Sable Island (Canada)	A	Bottlenose dolphin (liver, n = 26): Max: 1520 ng/g wet wt. Mean: 420 ng/g wet wt.	Florida
		Ringed seal (liver, n = 81): Max: 1100 ng/g wet wt. Mean: 240 ng/g wet wt.	Northern Baltic Sea
Survey of mammals, birds and fish in the Canadian Arctic	B	Polar bear (liver, n = 7): Max: > 4000 ng/g wet wt. Mean: 3100 ng/g wet wt.	Canadian Arctic

Description	Reference	Reported Highest Concentrations (Max, Mean)	Location
		Arctic fox (liver, n = 10): Max: 1400 ng/g wet wt. Mean: 250 ng/g wet wt.	
Survey of fish (US, Europe, North Pacific Ocean, Antarctic)	C	Fish (muscle, n = 172): Max: 923 ng/g wet wt. Mean. 40 ng/g wet wt.	Belgian estuary
		Carp (muscle, n = 10): Max: 296 ng/g wet wt. Mean: 120 ng/g wet wt.	US Great Lakes
Survey of fish-eating birds (US, Baltic Sea, Mediterranean Sea, Japanese coast, Korean coast)	D	Bald eagle (plasma, n = 42): Max: 2570 ng/mL Mean: 520 ng/mL	Midwest US
Survey of mink and river otter in the US	E	Mink (liver, n = 77): Max: 4870 ng/g wet wt. Mean: 1220 ng/g wet wt.	US
		River otter (liver, n = 5): Max: 994 ng/g wet wt. Mean: 330 ng/g wet wt.	US
Survey of oysters in the US (Chesapeake Bay & Gulf of Mexico)	F	Oyster (Whole body, n =77) Max: 100 ng/g wet wt. Mean: 60 ng/g wet wt.	US
Fish samples upstream and downstream of 3M facility in Decatur, Alabama, US	G	Fish (whole body): Mean (upstream): 59.1 µg/kg wet wt. Mean (downstream): 1,332 µg/kg wet wt.	Decatur, US
Swedish urban and background	H	Perch: 3 - 8 ng/g (urban sites in the vicinity of	Sweden (Lake Mälaren)

Description	Reference	Reported Highest Concentrations (Max, Mean)	Location
fish samples		municipal STPs); 20-44 ng/g in Lake Mälaren and near Stockholm	

Sources: A: 3M (2003a), B: Martin *et al.* (2004a); C: Giesy and Kannan (2001c) in 3M (2003a); D: Giesy and Kannan (2001b) in 3M (2003); E: Giesy and Kannan (2001d) in 3M (2003a); F: Giesy and Kannan (2001e) in 3M (2003); G: Giesy and Newsted (2001) in OECD (2002); H: Holmström *et al.* (2003).

Concentrations of PFOS in guillemot (*Uria aalge*) eggs from Stora Karlsö in the Baltic Sea have been measured retrospectively from 1968 to 2003 (Holmström et al, 2005). The results shown in Figure 2 display a trend of increasing concentrations since 1968 (17 – 623 ng/g).

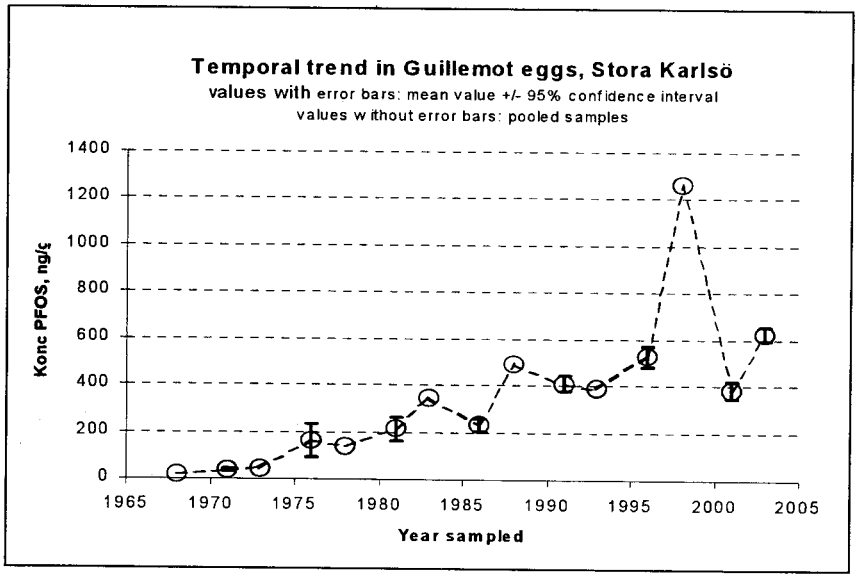

Figure 2. Measured concentrations of PFOS in Guillemot (*Uria aalge*) eggs sampled at Stora Karlsö in the Baltic Sea between the years 1968 – 2003. The graph is taken from the report "Screening av perfluorerade ämnen" by the Swedish EPA, Environmental Assessment Department (2004).

2.3.2 Bioavailability

Studies on fish have shown that PFOS has bioconcentration properties. In studies on bluegill sunfish (*Lepomis macrochirus*) and rainbow trout (*Oncorhynchus mykiss*), bioconcentration factors (BCFs) have been estimated to be 2796 (whole fish) as well as 2900 (liver) and 3100 (plasma), respectively. The major route of uptake is believed to be through the gills (Martin *et al.*, 2003).

Since PFOS is released from sewage treatment plants to the environment i.e. through water, one major route for PFOS into local food chains could be through fish. PFOS has shown a high oral uptake (95%) within 24 hours in the gastro-intestinal (GI) tract in studies on rats (OECD, 2002). Taken together, this could constitute the basis of the highly elevated levels that have been observed in top predators in food chains containing fish.

This could also be corroborated by two separate human monitoring studies on the Swedish population where the levels of PFOS in whole blood was higher (27.2 ng/g, 3.0 – 67, n = 10) in females with a high consumption of fish (Berglund, 2004) compared to samples from females in the general population (17.8 (ng/g, 4.6 – 33, n = 26) (Kärrman *et al.*, 2004).

In humans, the highest concentrations of PFOS have been detected in workers at 3M's manufacturing plant for perfluorochemicals in Decatur, US, where the levels in serum in the last year of measurement (2000) ranged between 0.06 – 10.06 ug/g (n = 263, OECD, 2002).

In a study of the general population, blood samples from families including three generations living in 12 European countries were tested for a large number of chemicals including PFOS and PFOSA. PFOS was present in 37 of 38 samples with concentrations from 0.36 to 35.3 ng/g blood, while PFOSA was present in 36 of 38 samples with concentrations from 0.15 to 2.04 ng/g blood (WWF, 2005).

Pooled serum samples from 3802 Australian residents, collected 2002-2003 and divided in relation to age, gender and region, were analysed for perfluoroalkylsulfonates, perfluoroalkylcarboxylates and PFOSA (Kärrman et al., 2006). PFOS and PFOSA were quantified in all pooled serum samples with a total range of 12.7-29.5 ng/ml (mean 17.2 ng/ml) and 0.36-2.4 ng/ml (mean 0.81 ng/ml), respectively. For PFOS, a significant correlation between age and concentration was shown. No substantial difference was found in levels of perfluorinated compounds between the urban and rural regions. According to gender some differences were shown for some of the age groups.

2.4 Hazard assessment for endpoints of concern

2.4.1 Mammalian Toxicity

Evidence of the mammalian toxicity of PFOS is available from acute, sub-chronic and chronic exposures to rats, sub-chronic exposures to monkeys, and a two-generation study on rats. Results are available from reproductive and teratogenicity studies on rats and rabbits. Details of these studies are not included here, they can be found in the assessment made by OECD (2002). The most relevant data for this risk profile are:

- A 90-day study on rhesus monkeys exposed to PFOS potassium salt via gavage at the doses 0, 0.5, 1.5 and 4.5 mg/kg bw/day. At 4.5 mg/kg bw/day all monkeys (4) died or were sacrificed in moribound condition. No deaths were observed at 0.5 or 1.5 mg/kg bw/day, but there were signs of gastrointestinal toxicity. A NOAEL could not be established since the lowest dose was a LOAEL (Goldenthal et al., 1978a).

- A 90-day oral repeated dose toxicity study in rats that were fed diets containing 0, 30, 100, 300, 1000 and 3000 mg PFOS potassium salt per kg diet. All rats died when fed diets containing 300 mg/kg PFOS and above (equivalent to 18 mg/kg bw/day and above). At 100 mg/kg (6 mg/kg bw/day), 50% (5/10) of the animals died. All rats receiving diets containing 30 mg/kg PFOS (2.0 mg/kg/day) survived until the end of the study, but small changes in body and organ weights were reported. Since the lowest dose tested was a LOAEL, a NOAEL could not be established (Goldenthal et al., 1978b).

- A two-generation reproductive toxicity study on rats that were fed PFOS potassium salt via gavage at the doses 0.1, 0.4, 1.6, and 3.2 mg/kg bw/day. At the doses 1.6 and 3.2 mg/kg bw/day a significant reduction in the viability of the F1 generation was observed. In the 1.6 mg/kg bw/day group, 34% (86/254) of the F1 pups died within four days after birth. In the 3.2 mg/kg bw/day group, 45% (71/156), of the F1 pups died within one day after delivery. None of these pups survived beyond day 4. Maternal toxicity at 1.6 and 3.2 mg/kg bw/day was manifested as reduced

food consumption, body weight gain, and terminal bodyweight. Localised alopecia was also observed at 3.2 mg/kg bw/day. The LOAEL in this study was 0.4 mg/kg bw/day based on significant reductions in pup weight gain in the F1 generation animals. The NOAEL was 0.1 mg/kg bw/day (Christian et al., 1999). A new study by Luebker *et al.* (2005) supports these results.

- Cynomolgus monkeys administered PFOS for 26 weeks were observed to have thymic atrophy (females), and reduced high density lipoprotein, cholesterol, triiodothyronine, total bilirubin levels (males) (Covance Laboratories, Inc. 2002a). The LOEL dose was 0.03 $mg.kg^{-1}$ bw/day at which average mean female and male concentrations in sera and liver were 19.8 $\mu g.mL^{-1}$ and 14.5 $\mu g.g^{-1}$, respectively.
- A 2-year dietary rat study in which histopathological effects in the liver were seen in males and females at intakes as low as 0.06–0.23 mg PFOS/kg bw per day and 0.07–0.21 mg PFOS/kg bw per day, respectively (Covance Laboratories, Inc. 2002b). Average values were determined for males and females to establish LOELs of 40.8 ug/g in liver and 13.9 mg/L in serum.

A study by Grasty *et al.* (2003) concluded that exposure of pregnant rats to PFOS late in gestation, at 25 mg/kg b.w. PFOS by oral gavage on gestation day (GD) 17-20 or 50 mg/kg PFOS on GD 19-20, is sufficient to induce 100% pup mortality and that the causative factor may be inhibition of lung maturation. However, in a subsequent study by Grasty *et al.* (2005), the mechanism behind pup mortality could not be established.

2.4.2 Ecotoxicity

Environmental toxicity data for PFOS is predominantly found for aquatic organisms such as fish, invertebrates and algae, and for birds.

PFOS has shown moderate acute toxicity to fish. The lowest observed LC_{50} (96h) was estimated to be 4.7 mg/l in a study where fathead minnow (*Pimephales promelas*) were exposed to the lithium salt of PFOS. The lowest NOEC, 0.3 mg/l, has been observed in *Pimephales promelas* at prolonged exposure (42d) and was based on mortality (OECD, 2002). The lowest LC_{50} (96h) for aquatic invertebrates has been observed in the mysid shrimp (*Mysidopsis bahia)* and was estimated to be 3.6 mg/l. The lowest NOEC value has been observed in *Mysidopsis bahia* at 0.25 mg/l (OECD, 2002).

A study by Macdonald *et al.* (2004) reported a 10-day NOEC of 0.0491 mg/L for the growth and survival of the aquatic midge (Chironomous *tentans*). The authors concluded that PFOS is 2-3 orders of magnitude more toxic to chironomids than to other aquatic organisms possibly through some kind of interaction with haemoglobin, which is present at all levels of dissolved oxygen (DO) in chironomids as opposed to daphnids, where haemoglobin is produced only in response to declining DO levels.

The most sensitive algae appear to be the green algae *Pseudokirchnerilla subcapitata* with a IC_{50} (96h, cell density) of 48.2 mg/L. The lowest NOEC value for algae was determined in the same study for *Pseudokirchnerilla subcapitata*, 5.3 mg/L (Boudreau *et al.*, 2003).

Mallard and bobwhite quail were exposed to PFOS in feed for up to 21 weeks and a variety of endpoints examined including changes in adult body and organ weights, feed consumption rate, fertility, hatchability, and offspring survival. At a dose of 10 mg/kg diet PFOS, effects in male mallards (*Anas platyrhyncos)* included reduced testes size and decreased spermatogenesis (3M, 2003b). At this dose, the concentrations of PFOS in serum and liver were 87.3 ug/mL and 60.9 ug/g, respectively (3M, 2004). For quail (*Colinus virginianus*), at 10 mg/kg in diet, minor effects were observed in adults, including an increase in liver weight (females), an increase in the incidence of small testes size (males), and reduction in survivability in quail chicks as a percentage

of eggs set. Concentrations in serum and liver of adult quail females was 84 $\mu g.mL^{-1}$ serum (week 5, pre-reproductive phase), and 8.7 $\mu g.mL^{-1}$ serum (week 21) and 4.9 $\mu g.kg^{-1}$ wet weight liver; in adult quail males, concentrations were 141 $\mu g.mL^{-1}$ serum and 88.5 $\mu g.g^{-1}$ wet weight liver (3M, 2003c).

3 SYNTHESIS OF THE INFORMATION

Perfluorooctane sulfonate (PFOS) is a fully fluorinated anion, which is commonly used as a salt in some applications or incorporated into larger polymers. Due to its surface-active properties, it has historically been used in a wide variety of applications, typically including fire fighting foams and surface resistance/repellency to oil, water, grease or soil. PFOS can be formed by degradation from a large group of related substances, referred to as PFOS-related substances (see definition on page 4).

Due to their intrinsic properties, PFOS and its related substances have been used in a wide variety of applications. While historically, PFOS and PFOS-related substances have been used in eight different sectors as shown in Section 2.1.2. above, the present use in industrialized countries seems to be limited to five sectors, see 2.1.2. It is not known whether this also reflects the global use.

PFOS and PFOS-related substances can be released to the environment at their manufacture, during their use in industrial and consumer applications and from disposal of the chemicals or of products or articles containing them after their use.

The rate and the extent of the formation of PFOS from its related chemicals are largely unknown. Lack of data makes it very difficult to estimate the net contribution of the transformation of each of the PFOS-related substances to the environmental loadings of PFOS. However, based on its extreme stability, it is expected that PFOS is likely to be the final degradation product of all PFOS-related substances.

PFOS is extremely persistent. It has not shown any degradation in tests of hydrolysis, photolysis or biodegradation in any environmental condition tested. The only known condition whereby PFOS is degraded is through high temperature incineration.

With regard to bioaccumulation potential, PFOS meets the Annex D criteria given the highly elevated concentrations that have been found in top predators such as the polar bear, seal, bald eagle and mink. Based on the concentrations found in their prey, high BMFs have been estimated for these predators. BCF values in fish, although (rather) high do not in themselves meet the specific numeric criteria. However, due to the properties of PFOS, which binds preferentially to proteins in non-lipid tissues, application of numeric criteria for BCF or BAF, which are derived based on consideration of lipid-partitioning substances, may be inappropriate for PFOS. Most notable and alarming are the high concentrations of PFOS that have been found in Arctic animals, far from anthropogenic sources. PFOS has been detected in higher trophic level biota and predators such as fish, piscivorous birds, mink, and Arctic biota. Also, predator species, such as eagles, have been shown to accumulate higher PFOS concentrations than birds from lower trophic levels. Even with reductions in manufacturing of PFOS by some manufacturers, wildlife, such as birds, can continue to be exposed to persistent and bioaccumulative substances such as PFOS simply by virtue of its persistence and long-term accumulation.

According to available data, PFOS meets the criteria for the potential for long-range transport. This is evident through monitoring data showing highly elevated levels of PFOS in various parts of the northern hemisphere. It is especially evident in the Arctic biota, far from anthropogenic sources. PFOS also fulfils the specific criteria for atmospheric half-life.

PFOS fulfils the criteria for adverse effects. It has demonstrated toxicity towards mammals in sub-chronic repeated dose studies at low concentrations, as well as rat reproductive toxicity with mortality of pups occurring shortly after birth. PFOS is toxic to aquatic organisms with mysid shrimp and *Chironomus tentans* being the most sensitive organisms.

Table 8. POP characteristics of PFOS (studies performed with the potassium salt of PFOS, unless otherwise noted).

Criterion	Meets the criterion (Yes/No)	Remark
Persistence	Yes	Extremely persistent. No degradation recorded in chemical or biological tests
Bioaccumulation	Yes	Found in highly elevated concentrations in top predators. Calculated hypothetical BMFs = 22 - 160. BCF in fish = 2796 - 3100.
Potential for Long-Range Environmental Transport	Yes	Atmospheric half life > 2 days (estimated value based on photolytic half life > 3.7 years)
Toxicity	Yes	Sub-chronic exposure: Mortality in monkeys at 4.5 mg/kg bw/day. Reproductive toxicity: mortality in rat pups at 1.6 mg/kg bw/day. Acute toxicity to Mysid shrimp (*Mysidopsis bahia)*: LC_{50} (96h) = 3.6 mg/L Acute toxicity to fish, Fathead minnow (*Pimephales promelas*): LC_{50} = 4.7 mg/L[1]

[1]The study compound was the lithium salt of PFOS

A risk quotient analysis, where known or potential exposures are integrated with known or potential adverse environmental effects, have been performed on PFOS for the wildlife in Canada (Environment Canada, 2006). The results indicate that the higher trophic level mammals may be at risk at current environmental concentrations of PFOS.

In the risk quotient analyses for polar bear, the highest concentration was found in South Hudson Bay with a maximum concentration of 3.77 $\mu g.g^{-1}$ ww liver (range 2.00-3.77 $\mu g.g^{-1}$, mean 2.73 $\mu g.g^{-1}$ ww liver, Smithwick *et al.* 2005). In comparing this value of 3.77 $\mu g.g^{-1}$ ww liver of PFOS in polar bear with a critical toxicity value of 40.8 $\mu g.g^{-1}$ ww liver for histopathological effects in liver

of rats (a 2-year study, Covance Laboratories, Inc. 2002), the difference is only about a factor 10. Using an application factor of 100[2], as was used in the Canadian Ecological Screening Assessment Report, a risk quotient of 9.2 was calculated, where values above one indicate risk. Risk quotients were also calculated on toxicological endpoints from other studies in rats and monkeys but with the same maximum exposure concentration from the south Hudson Bay polar bear, showing risk quotients from 2.1 to 19.

Concentrations in Canadian Arctic polar bear are among the highest in polar bears worldwide but the exposure concentrations are not considered an anomaly given similar concentrations in polar bears in other North America and European Arctic locations and high concentrations in other wildlife globally as shown above.

Risk quotients were also calculated for a number of bird species that are native to Canada, including many piscivorous birds and migratory species. The range of risk quotients is either above or approaching one that indicates potential for harm at concentrations observed in native species, including migratory species (Environment Canada, 2006).

4 CONCLUDING STATEMENT

PFOS is a synthetic substance of anthropogenic origin with no known natural occurrence. It can be concluded therefore that the presence of PFOS and its precursors in the environment are the result of anthropogenic activities and that PFOS found in remote areas far from possible sources has been brought there through long-range environmental transport. While PFOS related substances may be degraded to PFOS, PFOS itself is extremely persistent in all media and can bioaccumulate and biomagnify in mammals and piscivorous birds.

The voluntary phase out of PFOS production by the major producer in the USA has led to a reduction in the current use of PFOS-related substances. However, it can be assumed that it is still produced in some countries and it continues to be used in many countries. Given the inherent properties of PFOS,[3] together with demonstrated or potential environmental concentrations that may exceed the effect levels for certain higher trophic level biota such as piscivorous birds and mammals; and given the widespread occurrence of PFOS in biota, including in remote areas; and given that PFOS precursors may contribute to the overall presence of PFOS in the environment, it is concluded that PFOS is likely, as a result of its long-range environmental transport, to lead to significant adverse human health and environmental effects, such that global action is warranted.

[2] An application factor of 100 applied for extrapolation from laboratory to field conditions and for intraspecies and interspecies variations in sensitivity, and extrapolation from the observed effects level to a no-effect level.

[3] A decision on the inclusion of PFOS precursors has been postponed until the Committee has evaluated the information requested under Annex F.

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別添2

ペンタクロロベンゼンの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解しない(OECD TG 301C) 【光分解性】 大気中で、主として OH ﾗｼﾞｶﾙとの反応により光酸化される。日光照射下の表層水での分解は早く、4 時間で 41%が消失。 【半減期】 ・大気中:推定値は 45-467 日。OH ﾗｼﾞｶﾙとの反応による半減期の計算値は 277 日。ﾓﾃﾞﾙﾃﾞｰﾀに基づく半減期は 65 日。分解ﾌﾟﾛｾｽのみを考慮した場合の推定半減期は 155 日 ・水中:表層水中の推定半減期は 194-1250 日。更に深いところでの嫌気性生分解による推定半減期は 776-1380 日。 ・土壌中:ｽﾊﾟｲｸした下水汚泥改良土壌中で半量は揮発により素早く消失し、残り半量の半減期は 187-1550 日。好気性のﾛｰﾑ砂質土壌中の半減期は 194-345 日。湖水の砂状底質中で 150 日後に 75%が分解し、これに続く一次代謝物の半減期は 50 日。温帯地域の有機土壌と底質中の推定半減期は 6 年。	【ｵｸﾀﾉｰﾙ/水分配係数】 logKOW=4.88-6.12(推奨値 5.17-5.18) 【BCF(経鰓的生物濃縮係数)】 ・魚:BCF=1085-23000 ・軟体動物:BCF=833-4300 ・甲殻類:BCF=577-2258	【反復投与毒性】 [ラット 混餌:100 日] NOEL:18.2mg/kg/day(♀) LOEL:8.3mg/kg/day(♂) 8.3mg/kg/day 以上(♂)で腎重量増加、腎硝子滴 37.5mg/kg/day 以上(♀)で肝重量増加及び肝細胞肥大 81.1mg/kg/day(♂)及び 78.7mg/kg/day(♀)でヘモグロビン減少、白血球増加等 [ラット 混餌:13 週](NTP) NOEL:2.4mg/kg/day(♂)、 24mg/kg/day(♀) 2.4mg/kg/day 以上(♂)で絶対・相対肝重量増加、2.4mg/kg/day 以上(♀)で体重減少、7.2mg/kg/day 以上(♂)で組織学的所見を伴う腎重量増加、 24mg/kg/day(♂)以上で精子異常、小葉中心性肝細胞肥大、72mg/kg/day(♀)で腎毒性 【催奇形性】 ラット:50mg/kg/day の母体暴露で肋骨数過剰、胸骨異常の報告	【慢性毒性】 カダヤシ *Gambusia affinis* : 42dEC10=0.002 mg/L(成長) タイワンガザミ *Portunus pelagicus* : 40dEC10=0.014 mg/L(成長)

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Stockholm Convention on Persistent Organic Pollutants
Persistent Organic Pollutants Review Committee
Third meeting
Geneva, 19–23 November 2007

Report of the Persistent Organic Pollutants Review Committee on the work of its third meeting

Addendum

Risk profile on pentachlorobenzene

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on pentachlorobenzene, on the basis of the draft contained in document UNEP/POPS/POPRC.3/15. The text of the risk profile, as amended, is set out below. It has not been formally edited.

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PENTACHLOROBENZENE

RISK PROFILE

Adopted by the Persistent Organic Pollutants Review Committee
at its third meeting

November 2007

TABLE OF CONTENTS

EXECUTIVE SUMMARY

The European Community and its Member States being Parties to the Stockholm Convention have proposed pentachlorobenzene (PeCB) to be listed to the Convention. The Persistent Organic Pollutants Review Committee concluded that PeCB fulfilled the screening criteria set and decided to establish an ad hoc working group to review the proposal further.

Most of the countries who submitted information to the UNEP secretariat reported no production or use of PeCB (Czech Republic, Germany, Lithuania, Mauritius, Turkey, Canada), which is in agreement with the information in the dossier submitted. Past uses of PeCB are PeCB as a component in PCB products, in dyestuff carriers, as a fungicide and a flame retardant and as a chemical intermediate e.g. for the production of quintozene. Major U.S. and European manufacturers of quintozene have changed their manufacturing process to eliminate this use of PeCB. PeCB is also present at low levels as an impurity in several herbicides, pesticides and fungicides. In the United States, some pesticide manufacturers have changed their manufacturing processes to reduce the concentration of HCB impurities in their products, and these changes may have reduced concentrations of PeCB contaminants also. PeCB is also a low level degradation product of some pesticides. Literature sources show that PeCB is of no commercial significance. No trade or stockpiles have been reported.

Nowadays PeCB enters the environment through various sources of which PeCB as a byproduct of incomplete combustion is the largest current source. However, there is considerable uncertainty on the release of PeCB by various sources and available data are limited to the United States and Canada. The limited data available makes it difficult to provide a proper global estimate on amounts and trends. Total estimated annual global emissions of PeCBs based on the US-TRI database were 85.000 kg/yr.

PeCB should be considered as persistent given the estimated and experimental half lives in atmosphere, soils, sediments, and water. According to the available data PeCB has a high bioaccumulation potential. Log Kow values vary between 4.88 and 6.12, with recommended values of 5.17-5.18. BCF values range from 1085 - 23000 L/kg for fish, 833 – 4300 L/kg for mollusca, and 577 – 2258 L/kg for crustacea. Due to the fact that biotransformation of PeCB will be insignificant and the substance is very hydrophobic, the compound may also have a high biomagnification potential.
PeCB is moderately toxic to humans and is not classified as a carcinogen. Within the European Union PeCB is classified as a substance which is very toxic to aquatic organisms (LC50 for fish, daphnia or algae $\leq$ 1 mg/L). Limited data are available on terrestrial ecotoxicity and data for toxicity to birds are lacking.

Physical and chemical characteristics, such as water solubility, vapour pressure and Henry's Law Constant, are within the range of the other POPs. PeCB can be photo-oxidized in the atmosphere, largely through reactions with hydroxyl (OH) radicals. However, estimated half-lives of PeCB in air of 45 to 467 days were reported. Considering its physical and chemical characteristics and persistence in air, PeCB has a potential for long range transport through the atmosphere. This is supported by the presence of PeCB in environmental compartments, including biota, from remote regions.
PeCB is spread widely in the environment on a global scale. Measured levels of PeCB in abiotic and biotic media in remote regions such as the (ant) arctic environment are available, as well as monitoring data on PeCB in abiotic and biotic media of temperate zones. In general, data from developed countries indicates that concentrations of PeCB in the temperate zones of the world seem to decrease. For the (ant)arctic area, only recent data are available which do not allow to derive a trend.

Based on the available evidence, PeCB is likely, as result of its long range environmental transport, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

1 Introduction

The European Community and its Member States being Parties to the Stockholm Convention have proposed PeCB to be listed in Annex A, B and/or C to the Convention pursuant to paragraph 1 of Article 8 of the Convention. The complete original proposal is contained in document UNEP/POPS/POPRC.2/INF/5. A summary of the proposal prepared by the Secretariat was provided in document UNEP/POPS/POPRC.2/13.

The acceptance of the original proposal for further consideration by the Persistent Organic Pollutants Review Committee implies that the properties of the substance fulfilled the screening criteria set out in Annex D of the Convention. The next step is to prepare a risk profile for the substance as described in Annex E. This draft risk profile has been prepared following the decision of the Committee, at its second meeting in November 2006, to establish an ad hoc working group to review the proposal further in accordance with the provisions of the Convention (Decision POPRC-2/7).

All data in this document are presented according to the International System of Units (SI) and, therefore, many have been recalculated from other units in the data sources. Furthermore, all concentrations are presented based on kg or L (e.g. µg/kg or mL/L).

1.1 Chemical Identity of the proposed substance

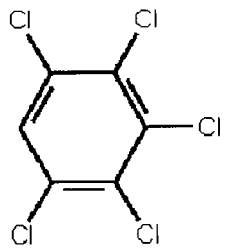
1.1.1 Names and registry numbers

PeCB belongs to the group of chlorobenzenes, which are characterised by a benzene ring in which the hydrogen atoms are substituted by one or more chlorines. The chlorobenzenes are neutral, thermally stable compounds with increasing stability and higher melting and boiling points with increasing chlorine substitution. PeCB has a very low solubility in water (Rossberg et al., 2006).

IUPAC Name: benzene, pentachloro-
CAS Chemical Name:
Synonyms: 1,2,3,4,5-pentachlorobenzene; Pentachlorobenzene; PCB; PeCB; QCB; quintochlorobenzene
CAS Registry Number: 608-93-5
EINECS Number: 210-172-0
Trade names: -

1.1.2 Structure

1,2,3,4,5-Pentachlorobenzene



1.1.3 Physico-chemical properties

Mackay et al (2006) provided a recommended value of 0.11 Pa at 20 °C. Water solubility at 25 °C varied between 0.135 and 3.46 mg/L, whereas the recommended value in various sources was around 0.55 mg/L. The log Kow values in Mackay et al (2006) varied between 4.88 and 6.12. This source and the PHYSPROP and CHEMFATE databases recommend values of 5.17-5.18 as most reliable. A full listing of the physical and chemical properties of PeCB is listed in Annex II, Table 1.1 in UNEP/POPS/POPRC.3/INF/21.

1.2 Conclusion of the Persistent Organic Pollutants Review Committee on the Annex D information on Pentachlorobenzene

At its second meeting on 6-10 November 2006, the POP Review Committee applied the screening criteria specified in Annex D to the Stockholm Convention, and concluded, in accordance with paragraph 4 (a) of Article 8 of the Convention, that it was satisfied that the screening criteria were fulfilled for PeCB. The Committee decided furthermore, in accordance with paragraph 6 of Article 8 of the Convention and paragraph 29 of decision SC-1/7 of the Conference of the Parties to the Stockholm Convention, to establish an ad hoc working group to review the proposal further and to prepare a draft risk profile in accordance with Annex E to the Convention. It invited, in accordance with paragraph 4 (a) of Article 8 of the Convention, Parties and observers to submit to the Secretariat the information specified in Annex E of the Convention before 2 February 2007.

1.3 Data sources

Information on the data sources (references and other literature) has been provided in UNEP/POPS/POPRC.3/INF/21 Annex I and III. Where the reviews mentioned above have been cited, the text quoted (or quoted with modifications) includes the references cited in the original review. These references are not shown individually in the reference list. The following parties and observers have answered the request for information specified in Annex E of the Convention: Canada, Czech Republic, Germany, Japan, Lithuania, Mauritius, Switzerland, Turkey, United States of America, International POPs Elimination Network (IPEN), and the International Council of Chemical Associations/World Chlorine Council (ICCA-WCC).

1.4 Status of the chemical under international conventions

PeCB is not included in any international convention. The European Commission has submitted a proposal to include PeCB to the Protocol to the 1979 Convention on Long Range Transboundary Air Pollution (LRTAP) on Persistent Organic Pollutants to the Executive Secretariat of the United Nations Economic Commission for Europe in 2006 (European Commission, 2007). The objective of the LRTAP POPs protocol is to control, reduce or eliminate discharges, emissions and losses of persistent organic pollutants. The UNECE Task Force on POPs identified the following options for possible inclusion of PeCB into the Protocol:
(a) Listing of PeCB in annex I to the Protocol in order to prevent production and use;
(b) Listing of PeCB in annex I and annex III to the Protocol. [ECE/EB.AIR/WG.5/2007/14]

PeCB is identified as a priority substance within the European Water Framework Directive (2000/60/EC). Within the list of these priority substances so-called priority hazardous substances are identified which are of particular concern for the freshwater, coastal and marine environment. These substances will be subject to cessation or phasing out of discharges, emissions and losses within 20 years after adoption of the Directive. The European Commission has proposed to include PeCB as a priority hazardous substance. [COM(2006) 397 final]. PeCB is listed on the OSPAR 1998 List of Candidate Substances (OSPAR, 1998).

2 Summary information relevant for the risk profile

2.1 Sources

Production, use and sources of release have been described extensively in the two documents submitted by Canada (Government of Canada, 1993, 2003), the proposed risk management strategy for PeCB by Canada (Environment Canada, 2005) and the document submitted by the ICCA/WCC (2007). Additional information was retrieved from the documents submitted by other Parties and Observers and from the open literature.

2.1.1. Production, trade, stockpiles

The submission document for PeCB reported that PeCB was not produced anymore within Europe and North America (Van de Plassche et al., 2002). PeCB has not been reported by EU Industry as an HPVC or LPVC (http://ecb.jrc.it/esis/). Most of the countries who submitted information to the UNEP secretariat reported no production (Canada , Czech Republic, Germany, Lithuania, Mauritius, Turkey, and USA). No intentional production was mentioned in the document submitted by the ICCA/WCC and according to Ullmann's Encyclopedia of Industrial Chemistry PeCB is of no economic significance (Rossberg et al., 2006). No trade or stockpiles have been reported.

2.1.2. Uses

Canada and the USA reported that there is no current domestic commercial demand for PeCB and that PeCB is not used as an end product. Ullmann's Encyclopedia of Industrial Chemistry does not mention any present use of PeCB (Rossberg et al., 2006). However, various past uses or unintentional uses of PeCB are mentioned in the literature:

1. PeCB was a component of a chlorobenzenes mixture used to reduce the viscosity of PCB products employed for heat transfer (Environment Canada, 2005), but new regulations prohibiting new uses of PCB-containing dielectric fluids resulted in a decline of the use of PeCB after 1980. PCBs are still in use in some old electrical equipment in North America and Europe so that there is a small potential for release of PeCB from this source (Environment Canada, 2005). It can be presumed that some PCBs are also still in use elsewhere in the world and some fraction of them contain PeCB. PCBs are being taken out of service in many countries of the world so that any related PeCB emissions are expected to decrease with time.

2. Formerly, PeCB and TeCB could be found in dyestuff carriers. The applications in dye carriers have been discontinued (Environment Canada, 2005). It is not clear from the Canadian document if PeCB, TeCB or both have been used in dyestuff carriers.

3. PeCB can be found as an impurity in several herbicides, pesticides and fungicides currently in use in Canada (Environment Canada, 2005). The US EPA carried out a study to assess the dietary cancer risk of hexachlorobenzene and PeCB as impurities in chlorothalonil, PCNB, picloram, and several other pesticides. PeCB was identified in pentachloronitrobenzene (quintozene), endosulfan, chlorpyrifos-methyl, atrazine, and clopyrilid, but not in simazine, chlorothalonil, picloram and dacthal (US EPA, 1998). Technical grade hexachlorobenzene (HCB) contains about 98 % HCB, 1.8 % pentachlorobenzene and 0.2 % 1,2,4,5-tetrachlorobenzene (WHO-IPCS, 1997). HCB is already listed in annex A and C of the Stockholm convention and it may thus be expected that HCB is of minor importance as a source for PeCB. The present situation for the other pesticides is unknown.

4. The use of PeCB as chemical intermediate is mentioned in WHO-IPCS (1991). So far, only the use as an intermediate in the manufacture of pentachloronitrobenzene (quintozene) has been found in the literature. PeCB is present as an impurity in this fungicide. Van de Plassche et al. (2002) report on the production and use of quintozene in various countries and indicated that the use outside the UNECE region is unknown. Van de Plassche et al. (2002) stated: 'Nowadays, quintozene is manufactured using another production process without PeCB. Amvac does not know of any current quintozene producer using PeCB as feedstock. They conclude that it is unlikely that there are any stockpiles of quintozene containing appreciable quantities of PeCB.' Feiler (2001) in ICCA/WCC (2007) reported that quintozene is now being made by chlorination of nitrobenzene instead of using PeCB as an intermediate. The available data suggest a decrease in PeCB use for the preparation of quintozene. However, this conclusion is based on data for Europe and North America only.

5. PeCB may have been used in the past as a fungicide and as a flame retardant (Van de Plassche et al., 2002). WHO-IPCS (1991) mentions that PeCB was formerly used in a pesticide to combat oyster drills. No further sources of these applications have been found.

6. Less than 0.1 kg per year of pure PeCB was imported into Canada from the United States for use as a laboratory reagent (Government of Canada, 1993). The use as laboratory reagent, based on data applicable to 1995, is also mentioned in Government of Canada (2003). The present situation is unknown.

From the data submitted and data in the literature it is obvious that production and use of PeCB in Europe and North America are negligible. The situation in other parts of the world is less clear.

2.1.3. Releases to the environment

The proposed risk management strategy for PeCB prepared by Environment Canada in 2005 mentions various routes through which PeCB can be released into the Canadian environment (Environment Canada, 2005). The main sources of release in Canada are barrel burning of house-hold waste , wood treatment plants and in service utility poles, pesticide use, dielectric fluid spill and cleanup, municipal solid waste incineration, hazardous waste incineration, magnesium production, solvent use and long range transport. As potential sources of release are mentioned: magnesium production (less than 2% of total annual releases), chlorinated solvents (negligible), secondary copper and aluminium processing (no data), chemical manufacturing (unlikely), iron and steel mills (scarcity of data), petroleum refineries (unlikely), wastewater treatment plants

(unlikely), textile mills (unlikely), long range transport (amount not known, expected to decrease) (Table 2.1, Annex II, UNEP/POPS/POPRC.3/INF/21).

The sources of release and potential sources are described more extensively in Environment Canada (2005). The total release provided by Environment Canada in the risk management strategy of PeCB (Environment Canada, 2005), 41.9 kg/yr, is a factor of 10 lower than the release of >580 kg/yr provided in the Priority substances list assessment report for PeCB (Government of Canada, 1993), submitted by Canada for the drafting of this Risk profile. The most significant sources in the Canadian risk management report (Environment Canada, 2005), barrel burning of household waste (21,93 kg/yr), municipal solid waste incineration (2.36 kg/yr), hazardous waste incineration (1.84 kg/yr) and magnesium production (1.53 kg/yr), were not identified as sources in 1993.

Data on releases of PeCB in the USA can be found in the U. S. EPA Toxics Release Inventory (TRI) (US EPA 2007a, http://www.epa.gov/tri/tridata/index.htm#pdr). The TRI contain release data for 2000 – 2004. Total releases vary between 1512 and 763 kg PeCB/yr and include air emissions, surface water discharges, underground injection, on site releases to land and transfers off-site to disposal. Air emissions between 2000 and 2004 were 74, 34, 37, 40 and 100 kg/yr respectively. Water emissions are in the same order of magnitude (See Table 2.2, Annex II, UNEP/POPS/POPRC.3/INF/21). The US also indicated in their comments that the data provided by TRI on "on-and-off-site releases" include amounts that would not be released to the environment because they were subject to treatment or other management activities. The TRI data does not cover all the industry sectors, which implies that total releases in the US can be much higher than those provided. Release data from other countries are not yet available.

The ICCA/WCC provided a document with an estimation of the annual global emissions of PeCB based on the U. S. Toxics Release Inventory (TRI) (ICCA/WCC, 2007). PeCB formation has been observed during combustion of municipal solid waste. The reported emission factors varied primarily due to differences in combustion conditions rather than fuel composition or waste content. The combustion of PVC may be a source of PeCB formation (Kim et al., 2004; Aracil et al., 2005; Muller et al., 1997), but the relative importance of this source is debated. There are other processes which produce a variety of chlorinated aromatics that may contribute to PeCB even if PeCB has not been explicitly detected and reported yet. Total estimated annual global emissions of PeCBs by ICCA/WCC (2007) were 85.000 kg/yr, about 2000 times the amount estimated for Canada and 850 times the total release of the United States. Most of the emission sources are similar with those provided in the Canadian risk management document (Environment Canada, 2005), but some are different. Hazardous waste incineration and wood treatment plants are lacking in the ICCA/WCC study, whereas combustion of coal and combustion of biomass, which amounts half of the total global emissions, are lacking in the Canadian study. Other PeCB sources could include quintozene degradation, titanium dioxide production, and ore treatment for the production of metals including magnesium, copper, niobium, and tantalum (ICCA/WCC 2007 citing Beck and Hansen, 1974; Knutzen and Oehme, 1989; Doering et al., 1992, and Vogelgesang 1986). No quantitative estimates are provided, because there is no quantitative information on which to base them. Although chemical manufacturing was thought to be unlikely as a source, the highest reported chlorobenzene concentrations in Canadian sediment have been observed near industrial sites (Government of Canada, 2003).

In conclusion, PeCB can enter the environment through various sources of which PeCB as a byproduct of incomplete combustion is the most significant current source. Nearly all fuels contain some chloride, especially biomass and waste. In industrial chlorination reactions it is possible that PeCB is produced as a byproduct and it probably accounts for some of the emissions reported. For a number of potential sources, such as copper and aluminum processing plants and steel mills no or limited data are available. From the data provided in the various documents one may expect a decrease of releases through past intentional use, due to phasing out of PeCB. In the case of unintentional releases as a byproduct of combustion a decrease can be expected in those cases where measures were taken to reduce the releases of other byproducts/emissions. The global estimate should be considered taking into account these uncertainties and the variation in industrial and waste handling processes among the various countries.

2.2 Environmental fate

2.2.1 Persistence

Pentachlorobenzene (PeCB) can be photo-oxidized in the atmosphere, largely through reactions with hydroxyl (OH) radicals (CEPA, 1993). There are no experimental data on atmospheric degradation, but the estimated half-life of PeCB is 45 to 467 days. For PeCB, the calculated half-life in air based on reaction with OH-radicals is 277 days (EPISUITE, US EPA, 2007b). Vulykh et al. (2005) estimate a half-life in air of 65 days based on modelling data. This estimate is the

result of degradation as well as dry and wet deposition and gaseous exchange with various surfaces. The atmospheric half-life of PeCB due to the degradation process only is estimated to be 155 days.

In the OECD TG 301C test PeCB was non-biodegradable (NITE, 2007). Photodegradation of PeCB is fast in surface water under sunlight irradiation: 41% loss after 24 hours (HSDB, February 2000). The half-life of PeCB in surface water was estimated to range from 194 to 1250 days, the estimated half-life for the anaerobic biodegradation in deeper water ranged from 776 to 1380 days (CEPA, 1993).

Wang et al. (1994) studied PeCB in spiked (4.5 µg/kg) and sewage sludge-amended soil (3 µg/kg) at 20-30 °C. Half of the dosage of PeCB is lost rapidly by volatilization, followed by degradation with half-lives of 187 days (spiked soil; 1.4 o.m.) to 1550 days (amended soil, 4.5% o.m.). Formation of bound residues is a relatively minor route of dissipation on soil. Scheunert et al. (1985) recovered 1% of a 2 mg/kg dosage as bound residue after 126 days. Under aerobic conditions PeCB is persistent in soil.

Beck and Hansen (1974) found disappearance half-lives based on duplicate samples, of 194 – 345 days in an aerobic loamy sand soil (1.9% o.m.); 18-20°C) treated at 7 mg/kg. Standard deviations were 20 to 25%. The 95% confidence limits are thus 112-726 and 289-3176 days. Since the values were based on duplicates, the total range of 112-3176 days represents the experimental results. Soils were kept in 10L buckets covered with two plastic sheets. During the experiment that lasted 600 days, water losses were compensated; apparently the total water content of the soil evaporated from the soils every 100 days (Bro-Rasmussen et al., 1970). The reported disappearance values are based on log(2)/k; instead of ln(2)/k. Correct half lives thus span the range of 260 – 7300 days. The contribution of volatilization of PeCB to these half lives is unknown.

Susarla et al. (1997) investigated the degradation of HCB in a methanogenic slurry of sandy sediment (<1% o.m.) with lake water (1:3 v/v), spiked at 1.14 mg/L. After 75% of the HCB had degraded after 150 days, the degradation of the primary metabolite PeCB followed first order kinetics with a half life of approximately 50 days at 25 °C. Masunaga et al. (1996) investigated the degradation of PeCB in sulfidogenic estuarine sediments that had been pre-exposed to various chemicals from local industries. Sediment slurries contained 272 g/kg solids; of which 12% can be lost by ignition, and were kept at 25°C. PeCB half-life was 18 days. In autoclaved samples the half-life was 990 days.

In sediment cores of Ketelmeer in The Netherlands, that had been selectively enriched with HCB to get a dechlorinating anaerobic community, PeCB is not persistent: the adapted anaerobic microflora gives half-lives of about 6 days at 25 °C when spiked at 50 µg/L (Beurskens et al., 1994). A mixture of clay loam soil (5.38% o.m.) and a sterile medium (50 g soil and 70 ml medium) was incubated anaerobically at room temperature after inoculation with a 10% slurry of an adapted microbial culture. The soil was spiked with 14.2 mg/L HCB, 25 mg/L PeCB, and 254.1 mg/L 1,2,4-TCB. Concentrations of PeCB decreased with a half-life of approximately 23 days. Chlorobenzene accumulated as the major metabolite after 80 and 142 days to 1 mmol/L (Ramanand et al., 1993). So far, only one bacterial strain which reductively dechlorinates chlorobenzenes has been isolated (Adrian and Görisch, 2002).

Comparison of PeCB concentrations in Ketelmeer sediment (The Netherlands) sampled and measured in 1972 to concentrations in samples taken in 1988 from sediment layers deposited around 1970, showed a small but statistically significant decline of 35%. HCB had decreased by 80%. Lower chlorinated benzenes like di- and tetrachlorinated benzenes had increased up to 80% (Beurskens et al., 1993). Lake Ketelmeer sediment contains 9-13% o.m. (Aarnoutse et al., 1996; Cornelissen and Gustafsson, 2004). In a UK soil (Woburn) that had received 25 separate sewage sludge applications in 20 years time (until 1961), approximately 21% of the added PeCB was still in the soil 30 years after application had stopped (Wang et al., 1995). This soil received about 25% of its dry weight in sludge. Assuming that sludge contained 80% organic matter and a 2% organic matter breakdown per year, the mean o.m. content was 15%. Input of HCB during these years was about 4 times higher than the PeCB input; and HCB residues also declined to 22% in these 30 years.

Experimental data on degradation of PeCB in water are lacking. PeCB is expected to dissipate from the water phase to the sediment or into the air. PeCB is persistent in soils and sediments under aerobic conditions. In anaerobic sediment-water slurries PeCB is considered persistent, except at temperatures above 10°C in combination with low organic matter contents. Higher organic matter contents seem to drastically increase the persistency. Actual field measurements of PeCB may overestimate persistency as a result of formation of PeCB from HCB. The true field half life of PeCB is estimated around 6 years in organic soil and sediment in the temperate zone.

PeCB should be considered as persistent given the magnitude 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.

2.2.2 Bioaccumulation

PeCB is highly hydrophobic. Mackay et al. (2006) report log K_{ow} values between 4.88 and 6.12, with recommended values of 5.17-5.18. Therefore, it can be assumed that the compound has a high bioaccumulation potential. This is confirmed by the data shown in Table 2.3, Annex II, UNEP/POPS/POPRC.3/INF/21 which summarizes values considered reliable according to the Klimisch criteria (Klimisch, 1997).

BCFs range from 1085 - 23000 L/kg for fish; 833 – 4300 L/kg for mollusca, and 577 – 2258 L/kg for crustacea. It should be noted that for the lowest BCF data for fish it is not explicitly clear if exposure concentrations have been measured (Schuler et al., 2007). If these BCFs are based on nominal instead of measured exposure concentrations, then they are probably lower than the 'real' BCFs based on measured concentrations.

In conclusion, these values show that PeCB can be considered to have a high bioaccumulation potential. Due to the high logK_{ow} and the fact that biotransformation may be insignificant (Schuler et al., 2006, 2007), the compound may also have a biomagnification potential. However, data on the biomagnification of PeCB are lacking.

2.2.3 Potential for Long range environmental transport

Overall persistence and long-range transport potential were estimated for five new POP candidates (including PeCB) with the OECD Pov & LRTP Screening Tool using the input properties in the POPRC proposal documents (Wegmann et al, 2007). The tool does not provide absolute levels in the environment, but facilitates comparison with earlier identified POP substances. The authors conclude that, although there are considerable uncertainties in the chemical characteristics of the five chemicals investigated, the POP candidates (including PeCB) have Pov and LRTP properties similar to those of several earlier identified POPs.

There is also evidence for long range transport of PeCB based on calculations of the transport distance of PeCB through the atmosphere. Mantseva et al. (2004) developed a multi-compartment transport model for the evaluation of long-range atmospheric transport and deposition of POPs. Based on this model assessment a transport distance in Europe of over 8 000 km is calculated for PeCB. The model is described in detail by Vulykh et al. (2005) who assessed a transport distance of 8 256 km. Based on measured concentrations in air samples of North America an empirical estimation of 13 338 km was made for the long rang transport of PeCB through air (Shen et al., 2005). This distance is larger than that of the other organochlorine pesticides that were part of this study including the currently listed POPs dieldrin, DDT and heptachlor.

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. In all air samples collected in 2000-2001 at the 40 sampling stations in North America (including 5 arctic stations), PeCB was detected. The measured concentrations were relatively constant across the continent, averaging 0.045 ng/m^3 with a range of 0.017 to 0.136 ng/m^3 (Shen et al., 2005). According to the authors, the small spatial variability across the Northern Hemisphere indicates that PeCB has a very long atmospheric residence time, which allows it to become widely distributed in the global atmosphere. The presence of PeCB has been reported in several abiotic (air, rainwater, water, sediment and soil) and biotic (fishes, birds, mammals) matrices at remote regions including the arctic region and Antarctica. These are described in detail in the section Exposure.

In conclusion, modeling, monitoring data of PeCB in air, as well as PeCB's chemical properties indicate that this substance has a considerable potential for long range environmental transport. The presence of PeCB in matrices from remote regions, some that can only have received PeCB after transport via air, supports the conclusion that PeCB is subject to long range transport.

2.3 Exposure

PeCB is spread widely in the global environment. The first two sections will focus on the levels of PeCB in abiotic and biotic media in remote regions such as the (ant)arctic environment. The third section will focus on monitoring data on PeCB in abiotic and biotic media of temperate zones, as well as observed trends. The last section discusses human exposure.

2.3.1 Levels in abiotic environmental matrices of remote regions

Atmospheric concentrations of PeCB have been measured at various locations around the world. Concentrations in air collected at Alert (Northwest Territories, Canada) ranged from 0.0031 to 0.135 ng/m^3 (Government of Canada, 1993). Measured concentrations across North America averaged 0.045 ng/m^3 with a range of 0.017 to 0.136 ng/m^3 (Shen et al., 2005). They also observed that atmospheric levels of organochlorine compounds including PeCB increased with increasing elevation in the Canadian Rocky Mountains.

PeCB was found in all water samples collected during a study of the distribution of chlorinated organics in the North Pacific Ocean, the Bering and Chukchi streets (ICCA/WCC 2007 citing Strachan et al., 2001). Concentrations of PeCB in the dissolved phase averaged 0.016 ng/L, while suspended solids represented only a small fraction of the total amount of PeCB. Bottom sediment samples taken from harbours in northern Norway and the Kola Peninsula in the arctic contained PeCB in concentrations ranging from 2 to 5 µg/kg dry weight. PeCB concentrations in four Alaskan arctic lakes sampled from 1991 to 1993 averaged 0.10 ±0.10 µg/kg dry weight (ICCA/WCC, 2007 citing Allen-Gil et al., 1997). Concentrations in soil samples from the coastal areas of Victoria Land (Antarctica) varied between 0.4 and 1.3 µg/kg dry weight (Borghini et al., 2005). In these soil samples PeCB was the dominant organic compound. Muir et al. (1995 as cited by ICCA/WCC, 2007) reported PeCB in sediment of a series of remote lakes in northern Canada. Sediment surface layer concentrations (representing a period of time estimated between 1979-1988) of PeCB in these northern lake ranged from less than 0.01 to 0.73 µg/kg sediment.

2.3.2. Levels in biota of remote regions

Contamination of the environment and biota in remote regions can be a threat to vulnerable species and ecosystems. PeCB is detected in mosses, fish, penguin eggs, seals and predatory mammals in the arctic and antarctic regions.

PeCB concentrations in mosses from coastal areas of Victoria Land (Antarctica) varied between 1 and 2.4 µg/kg dry weight (Borghini et al., 2005). The mosses do not have a root system and their supply is largely dependent on atmospheric deposition. The measured PeCB concentrations in both mosses were higher than those of the currently listed POPs HCB and DDT that were also included in this study. PeCB concentrations in mosses growing in the Andean Mountains at elevations between 700-4500 m ranged from 0.2 – 2.4 µg/kg dw (Grimalt et al., 2004). This study shows that PeCB is likely subject to cold-trapping. An inverse relationship was established with higher PeCB concentrations at lower temperatures. A similar relationship was established for mountain soils in Tenerife (Ribes et al., 2002).

Concentrations (µg/kg wet weight) of PeCB in organs from fish from Alaska and Northwestern Russia and other arctic locations varied between 0.06 ±0.08 and 5.06 µg/kg wet weight PeCB (ICCA/WCC, 2007 citing Allen-Gil et al., 1997, citing Muir et al., 2003, citing Arend et al., 2001, Vorkamp et al., 2004; Corsolini et al., 2006).

In Greenland PeCB was observed at levels of 23 µg/kg lipid weight in ptarmigan liver (1.5 µg/kg wet weight) and 8 µg/kg lipid weight in kittiwake muscle (1.1 µg/kg wet weight) (Vorkamp et al., 2004). Adelie penguin eggs (Antarctic) contained 0.68 µg/kg ww PeCB (Corsolini et al., 2006).

Inuit hunter collected tissue samples of ringed seals from the east and west sides of the Northwater Polnya between Canada and Greenland during the spring of 1998 (ICCA/WCC, 2007 citing Fisk et al., 2002). The concentration (wet weight) of PeCB in these sampled ranged from 7.3 ±1.9 µg/kg in male ringed seals to 8.4 ±1.1 µg/kg in females from the west side. Seals from the east side (Quebec) contained 5.0 ±0.5 µg/kg (males) and 7.0 ±1.5 µg/kg (females). Seals from the White Sea in Northwestern Russia collected in the period 1992-1998 contained PeCB at concentrations ranging from 0.9 (bearded seal) to 12.0 µg/kg lipid weight (harp seal) in their blubber (ICCA/WCC, 2007 citing Muir et al., 2003). The mean concentration (± standard deviation of the 10 samples) of PeCB in 1992 was 11±2.0 ng/g lipid weight whereas the concentration of PeCB in 1998 was 5.0±1.8 ng/g lipid weight. PeCB concentrations in bowhead whales collected between 1994 and 1998 averaged at 0.3 ± 0.1 and 0.8 ± 0.1 µg/kg wet weight in liver and blubber, respectively (ICCA/WCC, 2007 citing Hoekstra et al., 2002). St. Lawrence Bay (Canada) Beluga Whale blubber was found to contain 24.5 (1.56 – 1510) µg/kg (lipid weight) PeCB for females and 144.5 (1.5 - 1500) µg/kg for males (ICCA/WCC, 2007 citing Hobbs et al., 2003). In Greenland, blubber of musk ox (captured between 1998 and 2001) was reported to contain 0.32 µg/kg lipid weight PeCB (equivalent to 0.29 µg/kg ww) (Vorkamp et al., 2004).

PeCB has also been detected in polar bears. The compound was present in all 15 fat and plasma samples taken from polar bears from the arctic Svalbard islands (Gabrielsen et al., 2004) at an average concentration of 7.9 and a maximum of

13.9 µg/kg (wet weight). Similar concentrations are observed in polar bears from Alaska, Canada and East-Greenland, according to the authors. Concentrations and body burdens of chlorobenzenes (including PeCB) in polar bears of different ages have been studied before and after their seasonal fasts (ICCA/WCC, 2007 citing Polischuk et al., 2002). The authors conclude that no PeCB is metabolized or excreted during the fast, leading to increasing concentrations of the compound in fat tissue. Amounts of PeCB in cubs is reported to be greater than in adults due to the fact that nursing bear cubs receive an increased amount of PeCB.

The accumulation of PeCB has also been measured in the arctic fox during 1999-2001 (ICCA/WCC 2007, citing Hoekstra et al., 2003). The animals were collected some distance from human habitation to minimize effects of garbage scavenging. About 20 animals were collected at each site. PeCB concentrations (µg/kg) found in arctic foxes were0.61 ± 0.12 in muscle (Arivat), 0.29 ± 0.06 in muscle (Holman), 0.57 ± 0.11 in liver (Holman), 0.55 ± 0.20 in muscle (Barrow) and 0.73 ± 0.17 in liver (Barrow). Hoydal and Dam (2003) measured concentrations of <0.1 – 37 ng/g wet weight in biota captured in the environment of the Faroe Islands.

King et al (2003) studied the chlorobenzenes spilled after an accident in the Gulf of St Lawrence. There was a rapid decline in tri- to peCB concentrations in snow crabs from sampling location 1 [near the spill] between 1996 and 1998. From 1998 to 2000 the chlorobenzenes concentrations in snow crabs persisted at low levels. In 1996, chlorobenzenes concentrations at locations 2 to 11 were much lower than at location 1, but showed no consistent decrease with time.

2.3.3. Levels at temperate regions including trends

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 decrease. This pattern is representative for that of most POPs. For the (ant)arctic area, only recent data are available which do not allow to derive a trend.

A study of the influence of emission sources on atmospheric PeCB concentrations in Germany showed that concentrations were higher at industrial or urban locations (ranging from 0.057 to 0.286 ng/m^3) than at a rural reference site (0.031 ng/m^3) (ICCA/WCC 2007 citing Wenzel et al., 2006). Concentrations at the rural site are comparable to the average atmospheric concentration measured by the Integrated Atmospheric Deposition Network (IADN) above the North American Great Lakes in 2000, i.e., about 0.072 ng/m^3 (ICCA/WCC 2007 citing Buehler et al., 2004)

A clear trend of the presence of PeCB in the environment can be derived from its presence in sediment cores. Sediment cores from the industrially impacted area from Lake Ontario near the mouth of the Niagara River (Canada) show an increase in PeCB concentration from early 1900 until the period 1960-1970 (peak concentration of over 100 µg/kg) after which concentrations declined to about 10% of the peak concentration by 1980 (ICCA/WCC, 2007 citing Durham and Oliver, 1983 and NYDEC, 1998). Also PeCB concentrations in the Niagara river water dropped from 0.351 to 0.093 ng/L during the period 1987-1997 (ICCA/WCC 2007, citing Williams et al., 2000). However, data in the mussel watch programme for the Niagara river do not show a decrease in PeCB concentrations between 1997 and 2000 on several locations (Ministry of the Environment Ontario, 1999, 2003). Concentrations of PeCB in sediment of the Ketelmeer in The Netherlands dropped by 37% in the period 1972-1988 (Beurskens et al., 1993).

PeCB concentrations in Herring Gull eggs from Muggs Island / Leslie spit (Canada) have dropped from 50 µg/kg in 1970 to non-detected at 1 µg/kg in the mid 1990s (ICCA/WCC 2007, citing Bishop et al., 1992; Petit et al., 1994; Pekarik et al., 1998; Jermyn-Gee et al., 2005; Havelka, 2006). Calambokidis et al (1999) studied persistent pollutants in Harbor Seals (Phoca vitulina) in Puget Harbor (US) during the period 1984-1997. They concluded that total TEQ showed a near significant decline by year (p=0.07) and that other pesticides also showed general declining trends. Only for HCB, total chlorobenzenes, and chlordanes was the decline statistically significant. Only recent data (last 15 years) are summarized in Table 2.4 for abiotic and Table 2.5 for biota matrices in Annex II, UNEP/POPS/POPRC.3/INF/21.

During a survey within the Danube Regional Project for the European Water Framework Directive, PeCB was detected in almost all sediment samples at concentration levels of 0.0001 – 3.5 mg/kg and in most of the suspended solid samples at concentration levels of 0.001 – 0.028 mg/kg (Slobodnik and Dogterom, 2003). The ATSDR database from the US Government contains 41 records of polluted sites with PeCB. Maximum concentrations of PeCBs at these sites vary between 147 and 5100 mg/kg in sediments and between 0.43 and 2040 mg/kg in soil. Concentrations in fish vary between 0.00019 and 2.4 µg/g (ATSDR, 2007). Neither references mention if these concentrations are based on wet or dry weight basis.

2.3.4. Human exposure

Occupational exposure to PeCB may be through inhalation and dermal contact with this compound at workplaces where PeCB is produced or used. Examples are wood treatment plants, dielectric fluid spill and cleanup, municipal solid waste incinerators, hazardous waste incinerators, and magnesium production plants. Exposure may also arise in occupational settings where the pesticide quintozene is produced and used. The general population may be exposed to PeCB via inhalation of ambient air, ingestion of food and drinking water. Case reports of adverse effects in individuals, or epidemiological studies of populations exposed to PeCB have not been identified (Government of Canada, 1993).

PeCB has been detected in breast milk and found to accumulate in human placenta (Shen et al., 2007). The mean concentration of PeCB in the breast milk of Canadian women taken 3 to 4 weeks after parturition was < 1 µg/kg (trace) with a maximum value of 1 µg/kg. In this survey, the compound was detected in 97% of the 210 samples analyzed (detection limit and sampling period unspecified) (Government of Canada, 1993 citing Mes *et al.*, 1986). In the breast milk of women of Canadian indigenous population, "trace" (< 1 µg/kg) amounts of PeCB were observed in 17% of the 18 samples (detection limit not specified) (Government of Canada, 1993 citing Davies and Mes, 1987). Two other studies investigating PeCB in human milk reported concentrations in the range of 1 to 5 µg/kg (WHO-IPCS, 1991). PeCB has also been measured in abdominal, mammary, and perirenal fat tissue from 27 adult Finnish males and females (Smeds and Saukko, 2001). Workers with occupational exposure to PeCB were found to have higher levels of the substance in blood than control groups (Lunde and Bjorseth, 1977).

2.3.5. Bioavailability

The Environmental Health Criteria on chlorobenzenes (WHO/IPCS, 1991) concluded that limited evidence was available showing that sediment-bound residues of chlorobenzenes are bioavailable to organisms; i.e., aquatic invertebrates can take up residues from sediment, and plants, from soil. Since then, more information on the bioavailability of hydrophobic substances became available.

Bioavailability of chlorobenzenes is inversely proportional to the organic carbon content of the soil or sediment (Government of Canada (2003) citing e.g. van Gestel and Ma, 1988; Hulzebos et al., 1993). It was furthermore stated in the Canadian Follow-up Report that persistent substances can remain bioavailable for long periods of time, thereby increasing the probability and duration of potential exposure relative to compounds that do not persist in the environment.

It is generally accepted that not all fractions of organic pollutants bound on sediments or soils are equally toxic due to their various resistances to desorption. The resistant and sequestered fractions of PeCB are environmentally less harmful than the more readily desorbing, labile, or available fractions. The large fraction of water soluble organic matter in the sediments is potentially highly mobile and could be easily resuspended or leached to the overlying water column. If the soluble organic matter carries the major amount of PeCBs as expected, continuous contamination of the water body from the sediments is very likely. Qiao & Farrell (1996) carried out experiments with PeCB in rainbow trout and concluded that mass balance analysis suggests that the appearance of HCBP and PeCB in the fish after 6 days could not be accounted for solely by the amount of chemical dissolved in the water at the time when the fish were introduced. The chemical uptake in fish with the pharynx plugged, to eliminate the gut uptake route, was similar to that in control fish. Because direct access to bottom sediments did not alter chemical uptake, they concluded that hydrophobic chemicals such as PeCB and HCBP associated with suspended sediments from the Fraser River can readily desorb and be taken up across the gill. Åkerblom (2007) concluded that pesticide sorption to organic particles in standardized toxicity tests is fast and efficient and that substances bound to the sediment may act as a reservoir, continuously supplying the pore water with low pesticide concentrations.

As organic pollutants bound to sediment or organic matter may still become available, an evaluation should focus on sorption and desorption kinetics of PeCB and modifying circumstances rather than on statements on bioavailability. Such data are however scarce.

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.

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