別添8

商業用ペンタブロモジフェニルエーテルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 ・（Tetra, Penta, HexaBDE）難分解性（BIOWIN） ・（PentaBDE） 分解せず（OECD TG 301B で CO_2 発生なし） 【半減期】 ・大気中：11-19 日（EPIWIN） ・水中： 150 日（EPIWIN） ・土壌中：半減期 150 日（EPIWIN） ・好気性底質中： 600 日（EPIWIN） ・1970 年代初期にﾖｰﾛｯﾊﾟの海洋の底質に沈降した PentaBDE 同属体が現在も相当量存在しており、底質中での残留性が高いことが示されている。	【ｵｸﾀﾉｰﾙ/水分配係数】 log KOW=6.5-7.4 【BAF（経鰓及び経口による生物濃縮係数）】 ｾﾞﾌﾞﾗｶﾞｲ：BAF=1.8 【BMF（経口的生物濃縮係数）】 ・ｳﾐﾊﾞﾄ/ﾆｼﾝ：BMF=17 ・ﾊｲｲﾛｱｻﾞﾗｼ/ﾆｼﾝ：BMF=4.3 ・ｻｹ/ﾆｼﾝ：BMF=3.8 ・動物ﾌﾟﾗﾝｸﾄﾝ/底生生物：BMF=7.1 ・ﾎｯｷｮｸﾀﾞﾗ/動物ﾌﾟﾗﾝｸﾄﾝ：BMF=0.04-3.4 ・ﾜﾓﾝｱｻﾞﾗｼ/ﾎｯｷｮｸﾀﾞﾗ：BMF=13.7 ・ﾎｯｷｮｸｸﾞﾏ/ﾜﾓﾝｱｻﾞﾗｼ：BMF=0.3-11 ・多数の調査から、上位捕食者において懸念される濃度の PentaBDE が存在することが示されている。北極圏では、ﾜｼｶﾓﾒ、ﾎｯｷｮｸｸﾞﾏ、ﾜﾓﾝｱｻﾞﾗｼ、ｼﾛｲﾙｶなどの上位捕食鳥類および哺乳類中から高ﾚﾍﾞﾙの PentaBDE が検出されている ・土壌又は底質中のPentaBDEは、容易に食物連鎖に取り込まれ、人など食物連鎖上位者の脂肪組織中に生物濃縮する。	【反復投与毒性】 ラット（90 日）：NOEL 2mg/kg/day 未満 主な毒性は、肝臓肥大等（DE71） 【生殖毒性】 ラット（妊娠♀単回）：0.06mg/kg で児に自発行動変化（多動性） 0.3mg/kg で児に精巣体積・精子数の低値 （BDE99） 【催奇形性】 ラット（妊娠 6 日単回）：0.3mg/kg でばく露の母動物（F1）2 個体から得られた F2 児で、外観・骨格異常 （BDE99） 【その他】 実験動物で甲状腺ホルモン系への影響	【慢性毒性】 ミジンコ *Daphnia magna* ：繁殖阻害が認められた。

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

Addendum

Risk profile on commercial pentabromodiphenyl ether

At its second meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on commercial pentabromodiphenyl ether, on the basis of the draft contained in document UNEP/POPS/POPRC.2/7. The text of the risk profile, as amended, is provided below. It has not been formally edited.

PENTABROMODIPHENYL ETHER

RISK PROFILE

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

November 2006

CONTENTS

Executive Summary

A substantial range of studies on pentabromodiphenyl ether has been identified and the findings summarised in this risk profile. The new findings reported here support the conclusion reached by the Persistent Organic Pollutants Review Committee in 2005 that PentaBDE's properties fulfill the screening criteria in Annex D of the Stockholm Convention.

Commercial pentabromodiphenyl ether (C-PentaBDE) refers to mixtures of bromodiphenyl ether congeners in which the main components are 2,2', 4,4'- tetrabromodiphenyl ether (BDE-47 CAS No. 40088-47-9) and 2,2',4,4',5-pentabromodiphenyl ether (BDE-99 CAS No. 32534-81-9), which have the highest concentration by weight with respect to the other components of the mixture.

Commercial pentabromodiphenyl ether mixtures (C-PentaBDE) are used for flame retardant purposes as additives in consumer products. The commercial mixtures contain brominated diphenyl ether congeners with three to seven bromines in the molecule, but molecules with four and five bromines predominate. The proportion of the different polybromodiphenyl ether (PBDE) congeners in C-PentaBDE varies in different regions of the world.

PentaBDE is released into the environment during the manufacture of the commercial product, in the manufacture of products containing PentaBDE, during their use and after they have been discarded as waste. Even though production of C-PentaBDE is phased out or being phased out worldwide, different products containing it will still be in use in several years to come, resulting in continuing releases to the environment. The products will in the end of their lifetime become wastes with the potential of additional releases.

The main source in North America and Western Europe has been the C-PentaBDE incorporated in polyurethane foam, used in domestic and public furniture. This use is now mainly phased out. The information is too limited to draw conclusions on the importance of other uses, like textiles, electrical and electronic products, building materials, vehicles, trains and aeroplanes, packaging, drilling oil fluid and rubber products. While some representative examples are covered, detailed information on use is lacking for many regions of the world.

Major releases to air are emissions from products during use, through volatilization of PentaBDE and dust-borne PentaBDE. Emissions of PentaBDE can also occur from recycling and dismantling activities such as dismantling of vehicles, buildings and constructions. Emissions can occur from electronic waste recycling plants and shredder plants. Potentially toxic products such as brominated dibenzo-*p*-dioxins and furans might be generated during incineration of articles containing C-PentaBDE.

The releases of PentaBDE are to air, water and soil, but the major part ends up in soil. The distribution between the environmental compartments is: soil>>>water>air. Several studies using sediment cores show that PentaBDE is very persistent in marine sediments, still occurring after 30 years. In the main, PentaBDE in the environment is bound to particles; only a small amount is transported in its gaseous phase or diluted in water but such transport over long periods can be effective in distributing the PentaBDE widely in the environment, especially into Arctic regions. Occurrence in the Arctic environment is demonstrated in several monitoring studies in air and biota.

Due to its high persistency in air, the main route for long-range transport of PentaBDE - as with so many substances that are sufficiently volatile, persistent and bioaccumulative - is through the atmosphere. Modelling and environmental studies indicate that the transport is through a series of deposition/volatilization hops towards the poles but particulate transport is known to be important, too. Long-range transport through water and emigrating animals is also likely.

Several studies show that PentaBDE in soil and sediments is bioavailable, enters the food chain and that it bioaccumulates and biomagnifies in the food webs, ending up in high levels in top predators.

PentaBDE is widespread in the global environment. Levels of components of C-PentaBDE have been found in humans in all UN regions. Most trend analyses show a rapid increase in concentrations of PentaBDE in the environment and in humans from the early 1970s to the middle or end of the 1990s, reaching plateau levels in some regions in the late 1990s, but continuing to increase in others. The levels in North America and the Arctic are still rising. Vulnerable ecosystems and species are affected, among them several endangered species. Some individuals of endangered species show levels high enough to be of concern. Toxicological studies have demonstrated reproductive toxicity, neurodevelopmental toxicity and effects on thyroid hormones in aquatic organisms and in mammals. The potential for the toxic effects in wildlife, including mammals, is evident.

Potential exposure to humans is through food, and through use of products and contact with indoor air and dust. PentaBDE transfers from mothers to embryos and lactating infants. A Canadian assessment of risk quotients suggests that the highest risks accrue to species high in the food chain. Information is lacking on the effects in humans of short-term and long-term exposure, although it is to be expected that vulnerable groups can be pregnant women, embryos and infants. Considerably higher levels are found in humans from North America in general. About 5% of general populations have been found to be subjected to elevated exposure. This, together with the estimates of the long half-life of PentaBDE congeners in humans, raises concern for long-term effects on human health.

Based on the information in this risk profile, PentaBDE, due to the characteristics of its components, is likely, as a result of long-range environmental transport and demonstrated toxicity in a range of non-human species, to cause significant adverse effects on human health or the environment, such that global action is warranted.

1. Introduction

The Stockholm Convention is a global treaty to protect human health and the environment from persistent organic pollutants (POPs), of which twelve are currently listed under the Convention. POPs are chemicals that remain intact in the environment for long periods, become widely distributed geographically, accumulate in living organisms and can cause harm to humans and the environment. Norway, which is a Party to the Stockholm Convention, submitted a proposal in January 2005 to list pentabromodiphenyl ether in Annex A to the Stockholm Convention, and the POPRC agreed that the commercial product 'pentabromodiphenyl ether' ('PentaBDE') – actually a mixture as described below - met the screening criteria of Annex D to the Convention.

1.1 Chemical identity of the proposed substance

Commercial pentabromodiphenyl ether (C-PentaBDE) refers to mixtures of bromodiphenyl ether congeners in which the main components are 2,2', 4,4'- tetrabromodiphenyl ether (BDE-47 CAS No. 40088-47-9) and 2,2',4,4',5-pentabromodiphenyl ether (BDE-99 CAS No. 32534-81-9), which have the highest concentration by weight with respect to the other components of the mixture.

The numbering system for the PBDEs is the same as that used for polychlorobiphenyls (PCBs) (Ballschmiter *et al.* 1993).

The acronym PBDE is used for the generic term polybromodiphenyl ether, covering all congeners of the family of brominated diphenyl ethers. It is sometimes abbreviated to BDE.

1.2 Conclusion of the Review Committee regarding Annex D information

The Committee has evaluated Annex D information at its first meeting in Geneva in November 2005 (UNEP/POPS/POPRC.1/10) and has concluded that the screening criteria have been fulfilled for C-PentaBDE (Decision POPRC-1/3).

1.3 Data sources

This risk profile is elaborated using Annex E information submitted by countries and nongovernmental organizations, national reports from web sites for environment protection agencies in different countries, contact and submissions from Norwegian research institutes, the bromine industry, EMEP and AMAP.

Eleven countries have submitted information (Australia, Brazil, Canada, Japan, Norway, Mexico, Poland, Republic of Lebanon, Spain, Switzerland and United States of America). Seven countries submitted information on production and use. Only one country submitted information on releases; another reported that they did not have release data. All except one country provided monitoring data. There was no information on stock-piles from submitting countries and only a few have submitted information on trade. Two observers submitted information - World Wide Fund for Nature (WWF) and the International POPs Elimination Network (IPEN).

1.4 Status of the chemical under other international conventions

1.4.1 The OSPAR Convention

The Convention for the Protection of the Marine Environment of the North-East Atlantic (the OSPAR Convention) is guiding international cooperation on the protection of the marine environment of the North-East Atlantic. The OSPAR Convention was signed in Paris in 1992 and entered into force on 25 March 1998. The OSPAR Commission is made up of representatives of the Governments of 17 Contracting Parties and the European Commission, representing the European Community. In 1998, the OSPAR Commission placed PBDEs on its "List of Chemicals for Priority Action." An OSPAR

Commission background document on PBDEs was reviewed by Sweden in 2001. The next full review of this document is not planned before 2008. At the 4th North Sea Conference, it was decided to phase out the use of brominated flame retardants by 2020.

1.4.2 The UNECE Convention on Long-range Transboundary Air Pollution

United Nations Economic Commission for Europe (UNECE) works for sustainable economic growth among its 55 member countries. The UNECE Convention on Long-range Transboundary Air Pollution was signed by 34 Governments and the European Community in 1979 in Geneva. Under it, Parties shall endeavour to limit and, as far as possible, gradually reduce and prevent air pollution including long-range transboundary air pollution. It entered into force in 1983 and has been extended by eight specific protocols. There are today 50 countries that are parties to the Convention. The Protocol for persistent organic pollutants (POPs) was adopted on 24 June 1998 in Aarhus (Denmark). It focuses on a list of 16 substances that have been singled out according to agreed risk criteria, for total ban, elimination at a later stage or restrictive use. C-PentaBDE was nominated as a new POP to the Convention in 2004 by Norway. In December 2005 it was considered by the Executive Body of the Convention to meet the screening criteria for POPs, set out in EB decision 1998/2. They requested that the UNECE Task Force on POPs continue with the review and fuether explore management strategies..

1.4.3. The Rotterdam Convention

The Rotterdam Convention is a multilateral environmental agreement designed to promote shared responsibility and cooperative efforts among Parties in the international trade of certain hazardous chemicals. It is an instrument to provide importing Parties with the power to make informed decisions on which chemicals they want to receive and to exclude those they cannot manage safely.

The text of the Rotterdam Convention on the Prior Informed Consent Procedure for Certain Hazardous Chemicals and Pesticides in International Trade was adopted at the Diplomatic Conference held in Rotterdam on 10 September 1998. The Convention entered into force on 24 February 2004 and became legally binding for its Parties. Today there are 102 states that are parties to the Convention. The EU notified PentaBDE to the Rotterdam Convention in 2003. For it to become a candidate, bans of the substance must be notified by two parties under the Convention.

1.4.4 Other international forums of relevance

The Arctic Council is a high-level intergovernmental forum that provides a mechanism for addressing the common concerns and challenges faced by the Arctic governments and the people of the Arctic. Member states are Canada, Denmark (including Greenland and the Faeroe Islands), Finland, Iceland, Norway, Russia, Sweden and United States of America. Six international organizations representing many Arctic indigenous communities have the status of Permanent Participants of the Arctic Council.

Significant monitoring and assessment of pollution in the Arctic is performed under the auspices of the Arctic Council (The Arctic Monitoring and Assessment Programme, AMAP). This work is important in identifying pollution risks, their impact on Arctic ecosystems and in assessing the effectiveness of international agreements on pollution control, such as the Stockholm Convention on Persistent Organic Pollutants (POPs). AMAP has shown that PentaBDE is one of the important pollutants of the Arctic.

In the autumn of 2004, the Arctic Council adopted a new Arctic project concerning the reduction of brominated flame retardants. The project will be managed by Norway.

2. Summary information relevant to the risk profile

2.1 Sources

2.1.1. Production and use

Based on the last information on total market demand of C-PentaBDE presented at the Bromine Science and Environmental Forum (BSEF), the estimated cumulative use of C-PentaBDE since 1970 was 100 000 metric tons (tones). The total market demand decreased during the later years of this period, for example from 8,500 tons in 1999 to 7,500 tons in 2001 (BSEF, 2001).

Table 2.1. C-PentaBDE volume estimates: Total market demand by region in metric tons (BSEF, 2001).

	America	Europe	Asia	Rest of the world	Total
1999	8,290	210	-	-	8,500
2001	7,100	150	150	100	7,500

These consumption figures need to be seen in the context of the global demand for polybrominated flame retardants of all types, which vastly outweighs the demand for C-PentaBDE. Thus, world totals of PBDE were 204,325 (1999), 203,740 (2001), 237,727 (2002) and 223, 482 (2003) tonnes (BSEF 2006).

C-PentaBDE has been produced in Israel, Japan, U.S. and EU (Peltola *et al.* 2001 and van der Goon *et al.* 2005). Since 2001 actions to regulate or voluntarily phase-out C-PentaBDE have been conducted in several countries.

Production in EU ceased in the former EU (15) in 1997 (EU 2000). Usage in the EU (15) has been declining during the second half of the 1990s and is estimated to be 300 metric tonnes in 2000 (used solely for polyurethane production) (EU 2000). The use of PentaBDE was banned in the EU (25) in 2004. Use in electrical and electronic appliances ceased on 1 July 2006.

In the United States of America, in June 2006, the U.S. Environmental Protection Agency (EPA) issued a significant new use rule on tetra-octaBDE and any combinations of these chemicals resulting from a chemical reaction, which requires persons to notify EPA before commencing manufacture or import for any use. C-PentaBDE will be banned in the state of California from 2008. The sole US manufacturer voluntarily ceased production, but use may be continuing and will cease only when stocks are fully exhausted. Although a patent on production of C-PentaBDE was taken out in China as recently as 1999 for a PBDE mixture that differs from the traditional penta-mix, the substance is being phased out in that country. Remaining production in China is estimated as less than 100 MT/year and will cease in 2007 when the substance is banned in that country.

A major bromine producer in Israel, Israel Chemicals and Industrial Products (formerly the Dead Sea Bromine Group), declares in a public statement on its web site that their products do not contain PentaBDE. This aligns the producer with the ban in the EU, which is an important market for the company's flame retardants.

There is today no production in Japan. The use of C-PentaBDE was voluntarily withdrawn from the Japanese market in 1990 (Kajiwara et al. 2004). Some developing countries around the East China Sea are potential "hot spots" releasing PentaBDE into the marine environment (Ueno *et al.* 2004). Many industrial manufacturers of computers, television sets and other electric household equipment are situated in the coastal areas of Asian developing countries (Ueno *et al.* 2004). There are indications on a phase-out of C-PentaBDE in manufacture of new electrical and electronic products in the Asian region, although uses there were always subsidiary to the major uses in polyurethane foams. The extent of this is uncertain. Waste electric products used in developed countries have been exported to Asian developing countries, such as China, India and Pakistan. This waste material has been recycled for recovery of valuable metals (Ueno *et al.* 2004) and continuation of this trade can remain a source to PentaBDE releases. No restrictions have so far been implemented in developing countries in the Asia Pacific and the southern hemisphere.

The release of 'banked' PentaBDE during recycling of foam products has its parallel in the release of CFCs and other ozone depleting substances which have similarly remained in the foam during its useful lifetime.

Results from a survey of Canadian industries regarding certain substances on the country's Domestic Substances List conducted for the year 2000 indicated that no PBDEs were manufactured in Canada, but approximately 1300 tonnes of C-PentaBDE (for incorporation into finished articles) was imported into the country (Environment Canada 2003). Based on quantities reported, C-PentaBDE was the PBDE imported in greatest volume, followed by the commercial decabromodiphenyl ether product. A very small amount of octabromodiphenyl ether was imported in 2000. The volumes reported do not include quantities imported in finished articles. In 2004, it was proposed that PentaBDE be added to the Virtual Elimination list in Canada.

In the U.S. the sole producer voluntarily ended their production of C-PentaBDE in 2004. In 2001 alone, almost 70,000 metric tons of PBDEs were produced globally, almost half of which was used in products sold in the US and Canada. Before the phase-out in U.S. the majority of C-PentaBDE formulation produced globally was used in North America (>97 %). At the end of 2004 in the US, approximately 7.5% of the more than 2.1 billion pounds of flexible polyurethane foam produced each year in the US contained the C-PentaBDE formulation (Washington State 2005).

In Australia in 2004, the National Industrial Chemicals Notification and Assessment Scheme (NICNAS) advised that all importers were phasing out imports of PentaBDE by the end of 2005, and this was reconfirmed by the major importers in mid-2005.

C-PentaBDE is used or has been used in the following sectors (Alaee *et al.* 2003, Danish EPA 1999, EU 2000, Prevedouros *et al.* 2004b, Swiss Agency for the Environment 2002, Birnbaum and Staskel, 2004):

- Electrical and electronic appliances (EE appliances) – computers, home electronics, office equipment, household appliances and other items containing printed circuit laminates, plastic outer casings and internal plastic parts such as small run components with rigid polyurethane elastomer instrument casings.
- Traffic and transport – cars, trains, aircraft and ships containing textile and plastic interiors and electrical components.
- Building materials – foam fillers, insulation boards, foam insulation, piples, wall and floor panels, plastic sheeting, resins etc.
- Furniture – upholstered furniture, furniture covers, mattresses, flexible foam components.
- Textiles – curtains, carpets, foam sheeting under carpets, tents, tarpaulins, work clothes and protective clothing.
- Packaging – polyurethane foam based packaging materials.

The most common use, accounting for 95-98% of C-PentaBDE since 1999, has been in polyurethane foam (Hale *et al.* 2002). This foam may contain between 10 and 18% of the C-PentaBDE formulation. Polyurethane foam is mainly used for furniture and upholstery in domestic furnishing, automotive and aviation industry. Other uses are in rigid polyurethane elastomers in instrument casings, in epoxy resins and phenolic resins in electrical and electronic appliances, and construction materials. For some years now, the more highly brominated Deca-BDE has been preferred in these applications. C-PentaBDE has also been incorporated in minor amounts in textiles, paints, lacquers, in rubber goods (conveyer belt, coating and floor panels) and in oil drilling fluids. Levels range from 5-30% by weight. Up to the early 1990s, C-PentaBDE was used in printed circuit boards, usually FR2 laminates (phenolic resins) in Asia. Such FR2 laminates are used in household electronics (television, radio, video), vehicle electronics, white goods (washing machines, kitchen appliances, for example). In the early 1990s the amount C-PentaBDE used in textile treatment was 60 % of total use in the EU, but this application is now banned.

C-PentaBDE has been identified as an additive flame retardant in textiles in national substance flow analyses in the ECE region (Danish EPA 1999). Manufacturers of furniture textiles have stated that the textile contained 0.45% PentaBDE in a Norwegian flow analysis reported in 2003. Stringent rules on flammability apply to textiles used in the public sector, the transport sector and business sector, but rules for domestic use are less consistent.

According to information obtained from the bromine industry the use of C-PentaBDE as hydraulic fluid (as a component of a mixture) in petroleum borings and mining was discontinued 10-20 years ago.

Australia has reported uses in manufacture of polyurethane foams for refrigerators and packaging, and in epoxy resin formulations supplied into aerospace market and for use as potting agents, laminating systems and adhesive systems. The US has reported use of C-PentaBDE in the aircraft industry. There is no use of C-PentaBDE in newer aircraft, and thus no exposure of the public, but C-PentaBDE is still used in military aircraft.

2.1.2 Global demands for brominated flame retardants in the future

According to a market analyst consulting company, the global demand for flame retardants is expected to grow at 4.4% per year, reaching 2.1 million metric tons in 2009, valued at $4.3 billion. Growth will largely be driven by gains in developing countries in Asia (China, in particular), Latin America and Eastern Europe. Strong increases are forecast for most of the flame retardants. Globally, demand will be greatest for bromine compounds, due mainly to strong growth in China. Electrical and electronic uses will grow fastest. Higher value products will continue to make inroads as substitutes for less environmentally friendly compounds, especially in Western Europe, and chlorine compounds will begin to be replaced in China by bromine- and phosphate-based and other flame retardants (Fredonia Group 2005).

After a severe falloff in demand in 2001, electrical and electronic applications will continue to recover. Demand growth for flame retardants will be strongest in such applications. As electronic circuits become smaller, and more densely packed electronics are subjected to ever higher temperatures, the need for flame retardants will increase. Construction markets will be the second fastest growing globally, but in China second place will be held by motor vehicles, followed by textiles, both of which industries are growing rapidly in that country. Plastics will continue to replace other materials such as metals and glass in a wide range of products, in order to lower both cost and weight and to allow improved design and more flexible production. Plastic usage is already widespread and growing in fields such as transportation, building products and electronics. Plastics must be made flame retardant for many applications, and as a result some 75% of all flame retardants are used in plastics (Fredonia Group 2005).

Environmental restrictions vary by region. In Western Europe, Japan and to a lesser extent in North America, such restrictions will especially limit growth of chlorinated compounds. A ban on some brominated flame retardants in Western Europe is not expected to spread substantially to other regions, but it will drive the development of alternatives in electrical and electronic equipment for sale on the world market. Dozens of Asian, European and US companies announced in 2005 that they have developed or are developing electrical and electronic equipment that does not contain C-PentaBDE. In Asia, 51% of electronic manufacturers already make products compliant with the ban on PentaBDE in the EU, and 42% expected to have products that are compliant by 1 July 2006. Officials from electronics companies and industry consultants expected that the difficulty of keeping product streams separate would ensure that most electronic equipment sold on the world market would be compliant by 2005 (International Environment Reporter 2006).

2.1.3 Releases to the environment during production

PentaBDE is released into the environment during the manufacturing process, in the manufacture of products, during their use and after they have been discarded as waste. In addition to working towards a manufacturing process that does not cause emissions, it is also important to consider the contributions of emissions from products during use as well as after they have been discarded. Most of the PentaBDE is released as diffuse pollution during and after the service life of articles incorporating C-PentaBDE and as small-scale point source pollution from the waste management chain of the end products.

PentaBDE is synthesised from diphenyl ether by brominating it with elemental bromine in the presence of a powdered iron Friedel-Craft catalyst. The producers of PentaBDE have reported that the major routes of PentaBDE from this process to the environment are filter waste and rejected material, both of which are disposed of in landfills. Waste water releases of PentaBDE may also occur from spent scrubber solutions (Peltola *et al.* 2001).

According to the EU risk assessment of PentaBDE, the emissions in polyurethane production are assumed to occur prior to the foaming process, when handling the additives (discharges to water) and during the curing (emissions to air). Releases to air may occur during the curing phase of foam production, during which the foam stays at elevated temperature for many hours, depending on the production block size. Emission to air at this stage is estimated to be 1 kg/tonne PentaBDE, but it is assumed that some of the volatilized PentaBDE condenses in the production room and ends up in the waste water. The EU risk assessment concludes that 0.6 kg of PentaBDE is released in this way, and 0.5 kg into air, for each tonne of C-PentaBDE used in polyurethane foam production.

Table 2.2 Global production and use of C-PentaBDE in polyurethane foam production, and estimation of associated releases in 2000 (foam containing 10-18% PentaBDE).

Polyurethane foam production	**Quantity of PentaBDE**	**Release of PentaBDE into waste water**	**Emissions of PentaBDE to air during production**
150,000 tonnes/year	15,000-27,000 tonnes/year	9,000-16,200 kg/year	7,500-13,500 kg/year

An important source of release has been associated with the use of liquid flame retardant additives such as C-PentaBDE in production of polymer foams. Approximately 0.01% (that is, 100 g /tonne) of the raw material handled during mixing is estimated to be released to wastewater. There is also potential for release due to volatilization during the curing phase as described above, since foam reaches temperatures of 160°C for several hours. Wong *et al.* (2001) examined the atmospheric partitioning characteristics of BDEs 47, 99 and 153, and predicted that tetra- and pentabromo-congeners will become gaseous at warmer air temperatures. Therefore, although the low measured vapour pressure values for the PBDEs indicate that volatilization is minimal at normal air temperatures, there is potential for release to air at the elevated temperatures reached during curing (European Communities 2001). The European Communities (2001) study estimates the overall release of PentaBDE to be approximately 0.11%, with about one half of this going to air and the other half to wastewater.

2.1.4 Releases to the environment during product use

C-PentaBDE is used solely as an additive in physical admixture with the host polymer, and can thus migrate within the solid matrix and volatilize from the surface of articles during their life cycle (EU 2000). Approximately 3.9 % of the PentaBDE present in articles was estimated to be released each year through volatilization during their assumed service life of 10 years in the EU risk assessment, but each congener will have its own characteristic migration and volatility coefficients. Based on the quantities of shown in Table 2.2, and the 3.9% loss rate, it can estimated that 585-1053 tonnes of PentaBDE enters the environment in this way each year.

Wilford *et al.* (2003) conducted controlled chamber experiments in which they passed air through samples of C-PentaBDE -treated foam products containing 12% PBDE w/w. They found that PBDEs volatilized from polyurethane foam at measurable levels. Average total PBDE levels of 500 ng/m^3/g foam were released from the chamber. For BDE-47, BDE-99 and BDE-100 (4,5 and 5 bromines, respectively), the loss rates were 360, 85 and 30 ng/m^3/g foam, respectively. The average temperature range during sampling was 30-34°C.

Given the use of C-PentaBDE in domestic items such as furniture, carpeting and appliances, exposure to indoor air house dust containing PentaBDE has been examined in a number of studies (Shoeib *et al.* 2004, Wilford *et al.* 2005). US researchers (Stapleton *et al.* 2005) report results for a study conducted in 2004 in the Washington, DC, metropolitan area and one home in Charleston, South Carolina. The concentrations of PBDEs in house dust from sixteen homes ranged from 780 ng/g dry mass to 30,100 ng/g dry mass. The dominant congeners were those associated with C-PentaBDE and DecaBDE. It was estimated that young children (1-4 years) would ingest 120-6000 ng/day of PBDEs. For five of the homes, clothes dryer lint was also analyzed, showing PBDE concentrations of 480-3080 ng/g dry mass. The exposures are higher than those observed in Europe, a fact that the researchers attribute to the fact that most markets for C-PentaDBE has been in the United States.

The information in the preceding paragraph highlights the fact that while PentaBDE can volatilize from the products in which it is incorporated, as well as during their whole life-cycle, and during recycling or after disposal, a major route for dissemination of this chemical into the environment will be in the form of particles on which it is absorbed or adsorbed. When emitted from products, the flame retardants are likely to adsorb to particles, and these may adhere to surfaces within appliances or on other surfaces in the indoor environment, or they may spread to the outdoor environment during airing of rooms. Industrial environments where equipment is dismantled may suffer much higher exposures (Danish EPA 1999). There are also releases from products due to weathering, wearing, leaching and volatilization at the end of their service life during disposal or recycling operations (dismantling, grinding or other handling of waste, transport and storage, for example). The annual releases in the EU region from the product life-cycle of polyurethane products were estimated to be distributed among the different compartments as follows: 75% to soil, 0.1% to air and 24.9% to surface water (EU 2000).

The inclusion of C-PentaBDE in materials used for car undercoating, roofing material, coil coating, fabric coating, cables, wires and profiles, and shoe soles can result in slow release to the environment. Emission factors for such releases in the EU risk assessment were judged to be 2-10% during the lifetime of the product, with the higher factors applying to uses with high wear rates such as car undercoating and shoe soles. A further 2% was assumed to be emitted during disposal operations. Taking these into account, the losses in the EU region were estimated to be 15.86 tonnes/year to soil, 5.26 tonnes/year to surface water, and 0.021 tonnes/year to air. No actual measurements were found in the literature with which one might compare these estimates.

Hale *et al.* (2002) demonstrated that flame-retardant treated polyurethane foam exposed to direct sunlight and typical Virginia summer conditions with temperatures up to 30-35°C and humidity of 80% or greater, became brittle and showed evidence of disintegration within four weeks. The authors postulate that the resulting small, low density foam particles would be readily transportable by stormwater runoff or air currents. Such degradation processes may provide an exposure route to organisms via inhalation or ingestion of the foam particles and their associated PentaBDE.

2.1.5 Emissions from waste containing C-PentaBDE

Waste can be generated from production of C-PentaBDE, from processes for manufacture of C-PentaBDE -containing materials, and from end-of-service-life management of products containing PentaBDE.

In production, the C-PentaBDE producers have stated that the major source of release was from filter waste and reject material, but quantities are small to negligible. In general, the waste was disposed of to landfill (EU 2000), although it is noted that waste containing more than 0.25% PentaBDE is classified as 'hazardous waste'.

After curing and cooling, blocks of polyurethane foam generally have to be cut to the required size, although for some applications the foam is produced in a mould of the desired shape so cutting is not required. Some flame retardant is lost in the scrap foam that results from the cutting process. Such foam scrap is often recycled into carpet underlay (rebond), particularly in the United States. Interestingly, the EU exports about 40,000 tonnes/year of scrap foam to the US for such use (EU 2000). In other uses, scrap foam is ground and used as filler in a number of applications such as cars eats or used for addition to virgin polyol in slab foam production. It is also possible that some foam scrap will be disposed of to landfill, or even incinerated.

During the production of printed circuit boards a substantial part of the laminate is cut off and becomes solid waste. In most countries, however, C-PentaBDE is no longer used in this application. There is limited information about waste generated in other applications of C-PentaBDE, such as its use in electrical and electronic appliances. While some such appliances are recycled on account of their metal content, many are burned in municipal waste incinerators and this often the fate of non-metallic portions of this waste stream. In the EU, from December 2006, plastics containing brominated flame retardants must be separated from such waste prior to recovery and recycling.

Used vehicles, often containing solid or foam components with C-PentaBDE are stored outdoors and then dismantled in shredder plants. In some countries, restrictions require that components containing substances like PentaBDE be treated as hazardous waste. Wastes generated from production of building materials, textiles and furniture are disposed of in landfills, or incinerated. This is easy enough for small, easily dismounted components, but most material containing flame retardants is harder to segregate and so these materials end up in the waste from shredder plants and are usually landfilled.

Movement of polymer foam particles containing PentaBDE within the landfill could provide a mechanism for transport of the brominated material to leachate or groundwater. It is not currently possible to assess the significance of such processes. However, given the physico-chemical properties of the substance, it is considered unlikely that significant amounts of PentaBDE will leach from landfills, since it has low water solubility, high octanol-water partition coefficient, and adsorbs strongly to soils (EU 2000). Norwegian screening studies have found levels of PentaBDE of concern in landfill leachates (Fjeld *et al.* 2003, Fjeld *et al.* 2004, Fjeld *et al.* 2005). The quantity of PentaBDE disposed of annually in the EU, and going to landfill or incineration, is estimated to be approximately 1,036 tonnes (EU 2000).

In a Dutch project, the emissions of PentaBDE in the EMEP region were estimated and distribution between sources was as follows: 0.33 tonnes/year from industrial combustion and processes, 9.45 tonnes/year from solvent and product use and 0.05 tonnes/year from waste incineration (van der Gon *et al.* 2005).

At the operating temperatures of municipal waste incinerators almost all flame retardants will be destroyed, but based on experience with other organic compounds, trace amounts could be passing the combustion chamber (Danish EPA 1999). Studies of recipients to municipal solid waste incinerators have detected above-background levels of PentaBDE in both gaseous and particulate fractions in the air in the vicinity of the facility (Agrell *et al.* 2004, Law 2005, ter Schure *et al.* 2004b). Potentially toxic products like brominated dibenzo-*p*-dioxins and dibenzofurans may be produced during incineration of articles containing C-PentaBDE (Danish EPA 1999, Ebert and Bahadir 2003, Weber and Kuch 2003, Birnbaum and Staskel 2004) and possibly released to the environment.

Analyses of dismantled FR2 circuit boards in electrical scrap show that about 35% of the PBDE used was PentaBDE, and for estimation purposes it was assumed that 25% of FR2 laminates in older appliances had been treated with the C-PentaBDE (Swiss agency 2002). Prevedouros *et al.* (2004) estimated production, consumption, and atmospheric emissions of PentaBDE in Europe between 1970 and 2000 based on literature data. According to that study, the flow of PentaBDE in discarded electrical and electronic appliances in Europe is in the range 17-60 metric tons per year for the period 2000-2005. However, a Swiss experimental study of such flow in a modern recycling plant showed values higher than expected on the basis of the literature study. This could mean that the literature has under-estimated the PBDE content of such appliances, and the study acknowledges that companies seldom provide all the information necessary to make accurate estimates (Swiss agency 2002). This same study reported a flow analysis for the life cycles of Penta-, Octa- and Deca-BDE as well as tetrabromobisphenol A (TBBPA). Waste electrical and electronic equipment was the biggest contributor, ahead of automotive shredder residues and construction waste. The plastics in vehicles produced in 1980 contained 0.089 g/kg of PentaBDE (excluding that contained in electrical and electronic components), whereas plastic in those built in 1998 had 0.044 g/kg. At the beginning of this period, almost all unsaturated polyurethane resins were treated with brominated flame retardants, primarily DecaBDE and TBBPA, but also PentaBDE. Even larger quantities, up to 50 g PentaBDE/kg of resin, were used in rail vehicles produced in 1980.

The average concentration of PentaBDE in appliances is estimated to be 34 mg/kg, with the highest concentration – 125 mg/kg – in the plastic fraction (Morf *et al.* 2005). In plants with off-gas filtering, a large proportion of the PentaBDE will be found in the collected fraction (Morf *et al.* 2005). On the other hand, in a facility without an efficient air pollution control device such as that in the modern facility studied, a significant flow of dust-borne PentaBDE may be released to the environment. A case in point was presented by Wang *et al.* (2005), who detected levels of PentaBDE in soil and sediment collected in the vicinity of an open electronic waste disposal and recycling facility located in Guiyu, Guandong, China.

The Swiss study showed that 5% of polyurethane foams produced in 1990 were used in the building industry, and contained up to 220 g/kg of C-PentaBDE. About 10-20% of the thermoplastic sheeting used in construction was treated with brominated flame retardants at levels of 1.3-5% by weight (Danish EPA) but no information about C-PentaBDE content is available. Some polyvinyl chloride sheeting would also have been treated with C-PentaBDE, typically at 49 g/kg. PentaBDE can be assumed to be emitted during dismantling activities but no information is available about the extent of such emissions.

2.2 Environmental fate

2.2.1 Persistence

Estimated half-life values of PDBE in different environmental compartments are scarce in the literature. In table 2.3 half-life estimates found in literature are summarized.

*Table 2.3 Half-lives of PentaBDE (**BDE-99**) in different environmental compartments, estimated with the use of Syracus Corporation's EPIWIN program.*

Environmental compartment	**Half-life estimate (d)**	**References**
Soil	150	Palm 2001, Palm *et al.* 2002
Aerobic sediment	600	Palm 2001, Palm *et al.* 2002
Water	150	Palm 2001, Palm *et al.* 2002
Air	19 11	Palm *et al.* 2002 Vulykh *et al.* 2004

It is noted that caution should be used in relying on half-life estimates derived from this program, now called EPI Suite (http://www.epa.gov/opptintr/exposure/docs/episuite.htm). The EPI Suite's intended use is chemical screening only and may not be appropriate for consideration of substances for global control. Because of interest in this matter, it is likely that half-life data from new studies will be published but the picture provided by existing data seems unlikely to change substantially. The nature of degradation products of the PBDEs is also likely to be elucidated in future, leading to consideration of their toxicity.

With respect to biodegradation, Tetra-, Penta- and Hexa-BDE are predicted to be "recalcitrant" by the BIOWIN program. Using the EPIWIN program, estimated half-lives for PentaBDE are 600 days in aerobic sediment, 150 days in soil, and 150 days in water (Palm 2001). This degree of persistence is supported by the fact that no degradation (as CO_2 evolution) was seen in 29 days in an OECD 301B ready biodegradation test using PentaBDE (Schaefer and Haberlein 1997).

Schaefer and Flaggs (2001) carried out a 32-week anaerobic degradation study using a mixture of ^{14}C-labelled and unlabelled BDE-47 (a TetraBDE) incorporated into sediments. The study showed that <1% of the total radioactivity was recovered as $^{14}CO_2$ and $^{14}CH_4$, indicating that essentially no mineralization had occurred. Overall, the study found that levels of degradation were not statistically significant; however, the HPLC analytical method with radiometric detection indicated that some products had been formed in the 32-week samples. Between one and three such peaks were identified in 26 of 42 samples analyzed. Work is underway to identify these products. It is likely that BDE-47 has the potential to degrade very slowly under anaerobic conditions.

Several studies using sediment cores show that PentaBDE congeners deposited in European marine sediments at the beginning of 1970s are still present in significant amounts, indicating high persistency in sediments (Covaci *et al.* 2002a, Nylund *et al.* 1992, Zegers *et al.* 2000, Zegers *et al.* 2003). The industrial production and use in Europe started in the beginning of the 1970s, with a reduction in more recent years. This is reflected in the sediment core profiles, with no occurrence before this date, and an increase in levels after, with a levelling off in more recent years. In the most recent studies (Zegers *et al.* 2003) sediment cores from Norway, the Netherlands and Germany were studied. Concentrations of PBDEs, normalized to total organic carbon content, were in the range 10-20 µg/g total carbon.

2.2.2 Bioaccumulation

2.2.2.1 Studies on bioaccumulation and biomagnification in local food webs

Several studies have focused on PentaBDE's potential for bioaccumulation and biomagnification. The studies show an increase of concentrations in biota with increasing trophic level in pelagic and Arctic food webs. The calculated bioconcentration factors (BCFs), bioaccumulation factors (BAFs) and biomagnification factors (BMFs) indicate PentaBDE's potential for bioaccumulation and biomagnification. In Table 2.4 the calculated values in the literature are summarized. The octanol/water partition coefficient (log K_{OW}) for PentaBDE in those studies is 6.5 – 7.4. The more recent studies are described in the following text.

Table 2.4 Calculated bioaccumulation factors (BAFs) and biomagnification factors (BMFs) for one PentaBDE (BDE-99) in the literature from environmental studies in pelagic and Arctic food webs. The data are calculated using the mean lipid weight concentrations, except for the study performed by Sørmo et al. 2006, in which the values in brackets are BMFs calculated from mean whole body concentrations.

Variable	Organism	Area	Value	Reference
BAF	*Dreissena polymorpha*	Lake Mälaren, Sweden	1.8	Lithner et al. 2003
BMF	Guillemot egg/herring	Baltic sea	17	Sellström 1996
	Grey seal/herring	Baltic sea	4.3	Sellström 1996
	Salmon/sprat	Baltic sea	10	Burreau *et al.* 1999
	Salmon/sprat	Baltic sea	5.9	Burreau *et al.* 2000
	Atlantic Salmon/Small Herring	The Northern Atlantic Sea	3.8	Burreau *et al.* 2000
	Net plankton/Benthic organisms	Lake Ontario, Canada	7.1	Alaee *et al.* 2002
	Benthic organisms/Forage fish	Lake Ontario, Canada	0.8	Alaee *et al.* 2002
	T. libellula/Copepods	Svalbard, Arctic Norway	0.65 (1.3)	Sørmo *et al.* 2006
	G.wilkitzkii/Copepods	Svalbard, Arctic Norway	47.6 (19.0)	Sørmo *et al.* 2006
	Polar cod/Copepods	Svalbard, Arctic Norway	2.1 (1.6)	Sørmo *et al.* 2006
	Polar cod/*T. inermis*	Svalbard, Arctic Norway	1.9 (1.2)	Sørmo *et al.* 2006
	Polar cod/*T. libellula*	Svalbard, Arctic Norway	3.4 (1.3)	Sørmo *et al.* 2006
	Polar cod/*G.wilkitzkii*	Svalbard, Arctic Norway	0.04 (0.1)	Sørmo *et al.* 2006
	Ringed seal/*T. inermis*	Svalbard, Arctic Norway	26.8 (54.5)	Sørmo *et al.* 2006
	Ringed seal/*T. libellula*	Svalbard, Arctic Norway	43.1 (60.0)	Sørmo *et al.* 2006
	Ringed seal/*G.wilkitzkii*	Svalbard, Arctic Norway	0.6 (3.9)	Sørmo *et al.* 2006
	Ringed seal/Polar cod	Svalbard, Arctic Norway	13.7 (56.6)	Sørmo *et al.* 2006
	Polar bear/Ringed seal	Svalbard, Arctic Norway	0.3 (0.29)	Sørmo *et al.* 2006
	Polar bear/Ringed seal	Arctic Canada	3.4	Muir *et al.* 2006
	Polar bear/Ringed seal	Arctic Canada	11	Muir *et al.* 2006
	Polar bear/Ringed seal	Arctic Canada	8.0	Muir *et al.* 2006
	Polar bear/Ringed seal	Greenland	1.0	Muir *et al.* 2006
	Polar bear/Ringed seal	Svalbard, Arctic Norway	5.9	Muir *et al.* 2006

PBDE analyses of zebra mussels (*Dreissena polymorpha*) were included in a larger study undertaken in and around the city of Stockholm, Sweden (Lithner *et al.*, 2003). Mussels were collected from a background site and transplanted in baskets to other downstream sites in Lake Mälaren, Saltsjön and in several small lakes. Freshwater flows from Lake Mälaren, through the middle of Stockholm, then out into the brackish Baltic Sea via Saltsjön. Five PBDE congeners (BDE-47, BDE-99, BDE-100, BDE-153 and BDE-154) were determined. The congener pattern was dominated by BDE-47 and BDE-99 (four and five bromines, respectively) and was similar to the C-PentaBDE. Bioaccumulation factors (BAFs) for the various compounds studied were estimated using data from suspended particulate matter (SPM) collected in sediment traps in 1998-99 at the same sites in Riddarfjärden and Saltsjön (Broman *et al.*, 2001). The concentrations on SPM were assumed to reflect water concentrations. BAFs were calculated using lipid weight concentrations in mussels and organic carbon based concentrations in the SPM.

When compared to other compounds (PCBs, DDTs, HCB), the BDEs had the highest BAFs, ranging from 1 to 2. The BAF (= level in mussel/level in SPM) for PentaBDE was 1.8.

Concentrations of BDE-47 and BDE-99 in Lake Ontario pelagic food web show increasing concentrations with increasing trophic position (Alaee *et al.* 2002). In this study, concentrations of PBDEs in archived plankton, *Mysis*, *Diporeia*, alewife, smelt, sculpin and lake trout samples collected in 1993 were determined. The trophodynamics of PBDEs in the Lake Ontario pelagic food web were also investigated. Lake Ontario pelagic food web consists of three trophic levels. The lake trout (*Salvelinus namaycush*) is a top predator fish species in Lake Ontario, feeding on forage fish including alewife (*Alosa pseudoharengus*), rainbow smelt (*Osmerus mordax*) and slimy sculpin (*Cottus cognatus*); in turn these fish feed on *Mysis* and *Diporeia*, which feed on phytoplankton, and zooplankton sampled as net plankton. Concentrations were increasing at each step up the food chain. The exception to this trend was the biomagnification of BDE-99 from benthic organisms to forage fish, which had a biomagnification factor of 0.8. This is an indication of the breakdown of BDE-99. In fact, the PBDE profile in the plankton; *Mysis* and *Diporeia* resembled the C-PentaBDE formulation, which indicates that BDE-99 bioaccumulates in the invertebrates and starts to be metabolized by forage fish.

Further studies of metabolism involving reductive debromination are discussed in Section 2.3.5.

Whittle *et al.* (2004) conducted surveys of PBDE levels in fish communities of Lake Ontario and Lake Michigan in 2001 and 2002 and evaluated biomagnification in the local pelagic food web (net plankton/*Mysis*/*Diporeia* → forage fish (smelt/sculpin/alewife) → lake trout). Their analysis, which included a total of forty one PBDE congeners, showed that BDE 47, 99 and 100 were prominent at each trophic level. The biomagnification factors (BMFs) representing total PBDEs for forage fish to lake trout ranged from 3.71 to 21.01 in Lake Michigan and from 3.48 to 15.35 in Lake Ontario. The BMF for plankton to alewife as 22.34 in Lake Ontario.

A recent study of an Arctic food chain shows the same result (Sørmo *et al.* 2006) as Alaee's study. Concentrations of PBDEs were investigated in an Arctic marine food chain, consisting of four invertebrate species, polar cod (*Boreogadus saida*), ringed seals (*Pusa hispida*) and polar bears (*Ursus maritimus*). The most abundant PBDEs, BDE-47 and BDE-99, were found in detectable concentrations even in zooplankton, the lowest trophic level examined in this study. Most of the investigated PBDEs biomagnified as a function of tropic level in the food chain. A noticeable exception occurred at the highest trophic level, the polar bear, in which only BDE-153 was found to increase from its main prey, the ringed seal, indicating that polar bears appear to be able to metabolize and biodegrade most PBDEs. The authors suggested that this discrepancy in the fate of PBDEs among the different species may be related to greater induction of oxidative detoxification activities in the polar bear. Absorption and debromination rates may be more important for bioaccumulation rates of PBDEs in zooplankton, polar cod and ringed seals. BDE-99 showed no biomagnification from pelagic zooplankton to polar cod, probably as a consequence of intestinal or tissue metabolism of BDE-99 in the fish. Also among pelagic zooplankton, there was no increase in concentrations from calanoid copepods to *T. libellula*. Lipid-weight based concentrations (LWCs) and whole-body based concentrations (WBCs) of PBDEs were used to assess biomagnification factors (BMFs). Whole body concentrations gave the most realistic BMFs, as BMFs derived from LWCs seem to be confounded by the large variability in lipid content of tissues from the investigated species. This study demonstrates that PentaBDEs have reached measurable concentrations even in the lower trophic levels (invertebrates and fish) in the Arctic and biomagnifies in the polar bear food chain.

Polybrominated diphenyl ethers (PBDEs) were determined in adipose tissue of adult and sub-adult female polar bears sampled between 1999 and 2002 from sub-populations in Arctic Canada, eastern Greenland, and Svalbard, and in males and females collected from 1994 to 2002 in northwestern Alaska (Muir et al. 2006). Only four congeners (BDE-47, BDE-99, BDE-100, and BDE-153) were consistently identified in all samples. BDE-47 was the major PBDE congener representing from 65% to 82% of the

ΣPBDEs. Age was not a significant covariate for individual PBDEs or ΣPBDE. Higher proportions of BDE-99, BDE-100, and BDE-153 were generally found in samples from the Canadian Arctic than from Svalbard or the Bering- Chukchi Sea area of Alaska. All four major PBDE congeners were found to biomagnify from ringed seals to polar bears. The polar bear-seal BMFs were relatively consistent despite the large distances among sites. The exceptions were the BMFs for BDE-99, BDE-100, and BDE-153 in East Greenland which had lower BMFs than those at all other sites. This may imply differences in the transformation of PBDEs in the marine food web leading to polar bears or to food web differences. Species differences in bioaccumulation and biotransformation of PBDEs have been noted for fish and this could lead to differences in congener patterns in fish-eating mammals and their predators.

Studies of the biomagnification of Tri- to DecaBDEs were carried out in three different food chains, two in the Baltic Sea and one in the Atlantic Ocean (Law 2005). All of Tri- to HeptaBDE congeners biomagnified, but the maximum biomagnification was for the PentaBDEs.

Matscheko *et al.* (2002) investigated the accumulation of seven PBDEs, eight PCBs and polychlorinated dibenzo-*p*-dioxins and dibenzofurans (PCCD/Fs) by earth worms collected from Swedish soils in spring and autumn 2000. The selected sampling sites were agricultural lands receiving applications of sewage sludge, and a field flooded by a river known to contain the target substances in its sediment. Reference sites were rural and urban soils with no known sources of the target substances other than background. Earthworms (primarily *Lumbricus terrestris*, *Lumbricus spp*, *Aporrectodea caliginosa*, *A. rosea* and *Allolobophora chlorrotic*) were collected from all field sites, starved for 24 h to clear gut contents, and then analyzed for the presence of the target substances. Biota-soil accumulation factors (BSAFs) were calculated as the ratio of concentration of target substance in worm lipids to that in soil organic matter. BSAFs for BDE-47, BDE-66, BDE-99 and BDE-100 ranged from 1 to 10. They were comparable to those determined for the PCBs but higher than those for PCCD/Fs. BSAFs of greater than 10 were determined at one agricultural site, where factors of 11, 18 and 34 were calculated for BDE 99, 47 and 100 respectively. Data collected for BDE-153, BDE-154 and BDE-183 were not used, as levels in the earthworm blanks were deemed to be unacceptable high.

2.2.2.2 Monitoring results indicating bioaccumulation

A large range of studies show concentrations of concern in top predators. High levels in top predators are usually an indication on the potential of a compound to bioaccumulate in the top predator food chain.

Several studies (Jaspers *et al.* 2004, Herzke *et al.* 2005, Lindberg *et al.* 2004, D'Silva *et al.* 2004, Law *et al.* 2005, Sinkkonen *et al.* 2004, Sellström *et al.* 2003) indicate that PentaBDE is widespread in top predatory birds in Europe, such as peregrine falcon (*Falco peregrine*), merlin (*Falco columbarius*), goshawk (*Accipiter gentiles*), golden eagle (*Aquila chrysaetos*), and buzzard (*Buteo buteo*). High levels are detected in top predatory eggs of white-tailed sea eagle, peregrine falcon, osprey, and golden eagle (Herzke et al. 2005, Lindberg *et al.* 2004). High levels have also been detected in European harbour porpoises (*Phocoena phocoena*) (Thron *et al.* 2004 and Covaci *et al.* 2002).

In the Arctic, C-PentaBDE is detected in high levels in top predatory birds and mammals (Verrault *et al.* 2005, Verrault *et al.* 2004, Norström *et al.* 2002, Herzke *et al.* 2003, Vorkamp *et al.* 2004a and b, Wolkers *et al.* 2004, Thron *et al.* 2004, Thomas *et al.* 2005, Ikonomou *et al.* 2002), such as glaucous gulls (*Larus hyperboreus*), polar bears (*Ursus maritimus*), ringed seals (*Phoca hispida*) and beluga whales (*Delphinapterus leucas*).

2.2.3 Long-range environmental transport

2.2.3.1 Environmental studies on transport and distribution

There are several factors indicating long-range transboundary transport of PentaBDE in the environment. It has a high persistency in air, with a half-life of 11-19 days (Palm *et al.* 2002, Vulykh *et al.* 2004)). Monitoring studies have detected a widespread occurrence in the European atmosphere (ter Shure *et al.* 2004, Lee *et al.* 2004, Jaward *et al.* 2004, Harrad and Hunter 2004, Harrad *et al.* 2004) and Arctic (AMAP 2002 and AMAP 2005, Peltola *et al.* 2001).

Sampling of air in the Great Lakes region of North America was undertaken in 1997-1999 and reported by Strandberg *et al.* (2001). PBDEs, mainly BDE-47 and BDE-99, were detected in all samples from four locations, and there was little variation over the time period. PBDE concentrations ranged from 5 pg/m^3 near Lake Superior to about 52 pg/m^3 in Chicago. At the temperatures of collection, 20±3°C, approximately 80% of the tetrabromo congeners were in the gas phase, but 70% of the hexabromo congeners were associated with particles.

Results for the far-northern Pacific covered particulate matter collected in July-September 2003 from the Bohai Sea to the high Arctic, 37° – 80° N (Xin-Ming Wang *et al.* 2005). The dominant congeners were BDE-47, BDE-99, BDE-100 (all present in the commercial pentamix) and BDE-209, with concentrations falling from mid- to high-latitudes, probably resulting (according to the authors) from dilution, deposition and decomposition of the PBDEs during long-range transport. Total PBDE concentrations were in the range 2.25 – 198.9 pg/m^3 with a mean of 58.3 pg/m^3. The source of the PBDEs is believed to be the North American continent from which they distill to an Arctic 'cold trap'.

The emphasis on any assessment of the dispersal of PentaBDE into the environment has to be on long-range transport, specially to Arctic regions, but there also is a growing body of data on dispersal of the substance and related congeners within regions. Air sampling in Southern Ontario in the Spring of 2000, before bud burst, showed PBDE concentrations of 88-1250 pg/m^3, with the lighter congeners (DBE-17, -28 and -47) dominating (Gouin *et al.* 2002). The concentrations fell to 10-20 pg/m^3, a change that the researchers attributed to, firstly, enhanced levels caused by expiration from the winter snowpack, followed by possible sorption by emergent foliage. Other studies in Ontario (Harner *et al.* 2002) found air levels of total PBDE in the range 3.4-46 pg/m^3. In later work, organic films on indoor and outdoor windows in Southern Ontario were examined for their content of PBDEs by Butt *et al.* (2004). While the PBDE content was dominated by BDE-209 from the decabromo mixture, there were significant quantities of congeners deriving from the C-PentaBDE. Back calculation gave total PBDE concentrations in outdoor air of 4.8 pg/m^3 and 42.1 pg/m^3 for indoor air.

Jaward *et al.* (2004a) studied a total of 71 passive air samples using semi permeable membrane devices (SPMDs) for eight BDE congeners (BDE-28, BDE-47, BDE-49, BDE-75, BDE-99, BDE-100, BDE-153 and BDE-154) during a six week period in 2002 at remote/rural/urban locations across 22 countries in Europe. BDEs were detected in approximately 50% of the samples, and the equivalent ΣBDE air concentrations estimated from the passive sampler data ranged from 0.5 to 250 pg m^3. The focus of the most elevated concentrations was the UK, which has a history of PBDE production and has also been a major user of PBDE formulations due to stringent fire regulations within the country. The UK is clearly a regional source for BDEs to the European atmosphere and, in contrast, levels reaching Europe from the west (over the Atlantic Ocean) are low. Other high values were detected in urban centres in mainland Europe – samples from Athens, Bilthoven (Netherlands), Geneva, Milan and Seville, for example. Non-detectable/very low values occurred in remote/background sites, especially in Iceland, Ireland, Norway and Sweden, and values in Eastern Europe were generally low. BDE-47 and BDE-99 contributed ca. 75% to ΣBDE, similar to their proportion in the Bromkal 70-5DE C-PentaBDE.

In the US, high-volume samplers were used to examine concentrations of gaseous and particulate PBDEs at five sites (urban, semi-urban, agricultural and remote) from the Midwest to the Gulf of Mexico, every twelve days during 2002-2003 (Hoh and Hites 2005). The mean concentration of total PBDEs at the Chicago site was 100±35 pg/m^3, some 3-6 times higher than those at other sites and significantly higher than measurements made in 1997-1999 (Strandberg *et al.* 2001). The mean concentration of PentaBDE was 31 pg/m^3 at the Chicago site, some 2-4 times the values for other sites.

Fugacity model results indicate that PBDEs will largely partition to organic carbon in soil and sediment and that their persistence will be strongly influenced by degradation rates in these media (although these are not well known). Only a small proportion of PBDEs exist in air and water. If this is the case, it suggests that these compounds have limited LRAT potential (Prevedouros *et al.* 2004a, Gouin and Harner 2003). This corresponds with PentaBDE's affinity for carbon, low solubility in water (1.0 µg/L) and low vapour pressure (7.6 x 10^{-6} Pa). However, Gouin and Harner (2003) suggest that because of their physical–chemical properties, PBDEs may experience active surface–air exchange as a result of seasonally and diurnally fluctuating temperatures. Subsequently, this may result in the potential for LRAT of the PBDEs through a series of deposition/volatilization hops, otherwise known as the ‘‘grasshopper’’ effect. This assumption is supported by environmental data. Lee et al. (2004) detected atmospheric concentrations of BDEs at two rural/semirural sites in England, and one remote site on the west coast of Ireland in 2001 and in 2000, respectively. ΣBDE concentrations at Mace Head, Ireland, were 0.22 to 5.0 pg/m^3 with a mean of 2.6 pg/m^3 and were controlled primarily by advection. ΣBDE concentrations at Hazelrigg (NW England) were 2.8 to 37 pg/m^3 with a mean of 12 pg/m^3, and at Chilton (SW England) were 3.4 to 33 pg/m^3 with a mean of 11 pg/m^3. The congener profile was, on average, similar to that of the C-PentaBDE. At the two English sites in the summer, PBDE concentrations were strongly influenced by temperature, indicating that land/air exchange processes play an important role in determining atmospheric concentrations.

The concentrations of PBDEs were determined in soil samples collected along a latitudinal transect through the UK and Norway, at remote/rural woodland (both coniferous and deciduous) and grassland sites (Hassanin *et al.* 2004). Concentrations for ΣBDE ranged from 65 to 12,000 ng/kg dry weight. BDE congeners BDE-47, BDE-99, BDE-100, BDE-153 and BDE-154, covering the major constituents of the C-PentaBDE, dominated the average congener pattern in the soils. This was interpreted as evidence that transfer of the congeners from materials treated with the commercial product from source to air to soil occurs with broadly similar efficiency, and that there is little degradation of the congeners by processes acting either during atmospheric transport or within the soils themselves. There was evidence of latitudinal fractionation of the BDE congeners, with the relative amounts of BDE-47 and the lighter congeners increasing to the north (with increasing distance from source areas) while the proportion of BDE-99 and the heavier congeners decreased. Plots of BDE congener concentrations against percentage soil organic matter yielded different slopes for different congeners. Steeper slopes were generally observed for lighter congeners such as BDE-47, indicating that they have undergone some air-surface exchange (“hopping”), whilst those of heavier congeners such as BDE-153 were close to zero, indicating that they are retained more effectively by soil following deposition. A Japanese study detected seasonal variations in the partitioning of PBDEs between the gas and particulate phase. The fraction of particulate PBDEs was higher in samples collected in winter than those in the summer (Hayakawa *et al.* 2004). PentaBDE is expected to be transported in the environment mostly by being absorbed onto particles due to its low volatility, low solubility and high affinity for carbon compounds. There are results from environmental studies which indicate that PBDEs are transported on air borne particles, and that they are susceptible to wet deposition (ter Schure *et al.* 2004a, ter Schure and Larsson 2002). Further transport depends on the fate of the particles. Fate after depositions on land depends on the level of wind erosion, that can vary with the season. Fate after deposition into the sea depends on oceanographic processes, such as water layering and transport by currents in the surface layers.

Ter Schure *et al.* (2004a) collected air and atmospheric bulk deposition samples on the island of Gotska Sandön in the Baltic Proper during a 10 week period in autumn 2001. The sampling site was chosen because of its central position in the Baltic Sea, and because of the absence of local point sources of pollution. Ten PBDE congeners were determined (BDE-17, BDE-28, BDE-47, BDE-85, BDE-99, BDE-100, BDE-153, BDE-154, BDE-183 and BDE-209). The median ΣBDE concentration (ΣBDE is the sum of the concentrations of the congeners determined in each study) was 8.6 pg/m^3, and the BDEs were mainly associated with particles. A comparison to levels of PCB in the atmosphere indicated that, as PCB concentrations in Baltic air have been declining, the input of BDEs by atmospheric deposition to the Baltic Proper now exceeds that of the PCBs by a factor of almost 40 times.

BDEs were determined in precipitation falling in southern Sweden during a two week period in 2000 (ter Schure and Larsson, 2002). The particle-associated and "dissolved" phases were separated during sampling and 65 ± 18% of ΣBDE was found to be particle-associated. The volume weighted mean concentration of ΣBDE (nine congeners) in rain was 209 pg/l, and the total deposition rate was 2 ± 1 ng ΣBDE/m^2/day. The congener profile in both phases of the total deposition was dominated by BDE-209, and thereafter BDE-47, BDE-99 and BDE-183, representing inputs from all three commercial PBDE formulations. The authors found that particle associated BDEs are effectively removed during small precipitation episodes, and that particle scavenging was an important mechanism for the wet deposition of BDEs.

A model assessment of potential for long-range transboundary atmospheric transport and persistence of PentaBDE have been carried out by EMEP (Co-operative programme for monitoring and evaluation of the long-range transmission of air pollutants in Europe). The values of LRTP were considered to be strongly influenced by environmental processes, such as degradation, deposition, gas/particle partitioning, and gaseous exchange with underlying surface. The main process of removal from the atmosphere for the two congeners BDE-47 and BDE-99 was found to be deposition to land and seawater, 78% to land and 15% to sea for BDE-47 and 77% to land and 21% to sea for BDE-99. Only 7% of BDE-47 and 2% of BDE-99 was degraded. The calculated half-life in air was 7 days for BDE-47 and 11 for BDE-99. The findings showed a spatial distribution of BDE-47 that covers the Arctic, Europe, the Mediterranean Sea and northern Africa. BDE-99 spreads over longer distances and spreads to the Arctic, Atlantic Ocean, Asia and Africa. Transport distances (TD) were calculated for the two congeners. The TD was 2300 km for BDE-47 and 2800 km for BDE-99 (EMEP 2004).

Wania and Dugani (2003) examined the long-range transport potential of PBDEs using a number of models – TaPL3-2.10, ELPOS-1.1.1, Chemrange-2, and Globo-POP-1.1 – and various physical and chemical properties – for example, solubility in water, vapour pressure, log K_{OW}, log K_{oa}, log K_{aw}, and estimated half-lives in various media. They found that all models yielded comparable results, with tetrabromodiphenyl ether showing the greatest atmospheric transport potential and decabromodiphenylether the lowest. The researchers estimated a characteristic transport distance (CTD) ranging from 1113 to 2483 km for the tetrabromo, 608 to 1349 for the pentabromo, 525 to 854 for the hexabromo, and 480 to 735 for the decabromo congener. The CTD was defined as the distance a parcel of air has travelled until 1/*e* (approximately 63%) of the chemical has been removed by degradation or deposition processes (Gouin and Mackay 2002).

The EU risk assessment (EU 2000) concluded that the major part of releases end up in soil. From soil, PentaBDE can be expected to be moved mainly through leaching with water in the suspended solids fraction or through wind erosion where it occurs. A small part in the soil can be volatilized, especially in the warm season, and so may be considered a plausible alternative mechanism for transport in addition to volatilization and advective transport of vapor identified in the literature. Although PentaBDE has low water solubility, it has been detected in lakes and seas, and can be transported with water in the soluble and particle phases (Peltola *et al.* 2001). Occurrence in migratory birds and fish indicate the possibility of transport by migration of animals, but the main route seems to be through the atmosphere.

2.2.3.2. Levels in remote areas

The detected levels in the Arctic atmosphere, biota and environment are strong indicators of the PentaBDEs potential for long-range transport (Verreault *et al.* 2005, Verreault *et al.* 2004, Norstrøm *et al.* 2002, Herzke *et al.* 2003, Vorkamp *et al.* 2004a and b, Wolkers *et al.* 2004, Thron *et al.* 2004, Thomas *et al.* 2004, Ikomomou *et al.* 2002, Christensen *et al.* 2002, de Wit *et a*l. 2004, AMAP 2002 and AMAP 2005).

There are several studies showing the occurrence of PentaBDE in remote areas in Europe as well (Vives *et al.* 2004, Hassanin *et al.* 2004 and Zenegg *et al.* 2003). Levels in remote regions are considered to be an indication on long-range transport.

PentaBDE (as total BDE) has been detected in Canadian and Russian Arctic air at concentrations up to 28 pg/m^3 (Alaee *et al.* 2002). Strandberg *et al.* (2001) reported concentrations of total PBDE (BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, BDE-190 and BDE-209) in air from the Great Lakes area during the period 1997-1999. Average concentrations based on four samples from each of four locations ranged from 4.4 pg/m^3 near Lake Superior in 1997 to 77 pg/m^3 in Chicago in 1998. The average air concentration of total PBDEs (1997, 1998 and 1999) for the sampling sites ranged from 5.5 to 52 pg/m^3. Tetra- and pentabromo congeners accounted for approximately 90% of the total mass of PBDE in this study. At 20±3°C, about 80% of the tetrabromo congeners and 55-65% of the pentabromo congeners were in the vapour phase while about 70% of the hexabromo congeners were associated with the particulate phase.

A larger study was performed detecting BDEs in trout (three species) from eleven high mountain lakes in Europe (566 to 2,485m altitude) (Vives *et al.*, 2004). These lakes were selected as being far from local pollution emission sources, and it was considered that the only source of BDEs to these lakes was as a result of atmospheric transport and deposition. The major congeners identified (of 39 determined) were BDE-47 and BDE-99, followed by BDE-100, BDE-153, BDE-154 and BDE-28, and these congeners were found in all samples analysed. The highest concentrations of ΣBDE in fish muscle and liver were found in Lochnagar, Scotland, 1.2 and 11 μg/kg wet weight, respectively (177 and 366 μg/kg on a lipid basis). No correlation was observed between the occurrence of these compounds and altitude, latitude or temperature, and the authors inferred that the environmental distribution of the BDEs has not, as yet, reached a steady-state.

2.3 Exposure

2.3.1 Levels

PentaBDE has spread widely in the global environment. A large quantity of monitoring data exist with detected levels in marine and terrestrial birds, sea and terrestrial mammals, sediments, soil, seafood and fish. A global study by Ueno *et al.* (2004) of PentaBDE in skipjack tuna (*Katsuwonus pelamis*) shows a wide spread occurrence in the offshore waters of various regions in the world. Table 2.5 gives an overview over the levels found in different parts of the world.

Contamination of the environment and biota in remote regions can be a threat to vulnerable species and ecosystems. In the Arctic, together with other pollutants of concern, PentaBDE is detected in high levels in top predatory birds and mammals (Verreault *et al.* 2005, Verreault *et al.* 2004, Norstrøm *et al.* 2002, Herzke *et al.* 2003, Vorkamp *et al.* 2004a and b, Wolkers *et al.* 2004, Thron *et al.* 2004, Thomas *et al.* 2004, Ikomomou *et al.* 2002) showing that the Arctic food webs are seriously affected. Wolkers *et al.* (2004) detected levels of PentaBDE in beluga whales (*Delphinapterus leucas*) in the Arctic, a species protected by the Convention on migratory species (the Bonn convention). ΣBDE concentrations (geometric mean; 22 congeners) were 234, 161 and 29 μg/kg in juvenile, adult male and adult female beluga.

In fact, there are detected high levels of PentaBDE in several species, with populations of concern protected by the Bonn convention. Several studies (Jaspers *et al.* 2004, Herzke *et al.* 2005, Lindberg *et al.* 2004, D`Silva *et al.* 2004, Law *et al.* 2005, Sinkkonen *et al.* 2004, Sellström *et al.* 2003, Kannan *et al.* 2005, Ramu *et al.* 2005 and Wolkers *et al.* 2004) indicate that PentaBDE is widespread in peregrine falcon (*Falco peregrine*), merlin (*Falco columbarius*), goshawk (*Accipiter gentiles*), golden eagle (*Aquila chrysaetos*), buzzard (*Buteo buteo)*, beluga whales (*Delphinapterus leucas*), irrawaddy dophins (*Orcaella brevirostris*), and Indo-Pacific humpback dolphin (*Sousa chinensis*), all protected by the Bonn convention. High levels of PBDEs are also detected in peregrine falcon eggs in Sweden (Lindberg *et al.* 2004), for which individual ΣBDE concentrations were as high as 39,000 µg kg^{-1} lipid weight, some of the highest concentrations seen in wildlife so far.

The populations of harbour porpoises (*Phocoena phocoena*) in the North and Baltic seas are protected through the Bonn Convention. Studies have detected high levels in those populations (Thron *et al.* 2004 and Covaci *et al.* 2002). In a study by Thron *et al.* (2004) animals with poor body condition (lower mean blubber thickness) had much higher concentrations than other individuals. Only females showed decreasing concentrations with age, indicating elimination via transfer from mother to offspring.

The harbour porpoise is, together with peregrine falcon and merlin, also on the list for strictly protected (endangered) species in the convention on the conservation of European wildlife and natural habitats (the Bern Convention). The white-tale sea eagle is on the list for endangered species in the Bern Convention. Levels of concern are detected in both individuals and eggs (Herzke *et al.* 2005). Beluga whales and irrawaddy dolphins are on list for protected (vulnerable) species. High levels are found in white-beaked dolphin (*Lagenorhyncus albirostris*), another endangered species. The parties of this convention undertake to take appropriate measures to ensure the conservation of endangered and vulnerable species and their habitats.

Table 2.5 Levels of PentaBDE ***(BDE-99)*** *in different parts of the world (LW=Lipid weight, DW=Dry weight).*

Country/Region	**Organism/compartment**	**Levels of PentaBDE**	**References**	**Comments**
Europe	Atmosphere Gas phase	10-120 pg/m^3	Jaward *et al.* 2004	22 countries
Japan	Atmosphere Particulate Gas phase	0.05-0.9 pg/m^3 0.05-19' pg/m3	Hayakawa *et al.* 2004	Measured in the summer
Sweden	Sediments	<0.7-51.4 ng/g DW	Palm *et al.* 2002	Rivers at point source
United Kingdom	Soil	78 – 3200 pg/g DW	Hassanin *et al.* 2004	
Western Europe	Sediments	<0.2-6.9 ng/g DW	Palm *et al.* 2002	Estuaries
Japan, Osaka	Sediments	9-28 ng/g DW	Palm *et al.* 2002	
North Pacific Ocean	Skipjack tuna	0.18-2.1 ng/g LW	Ueno *et al.* 2005	
Japan	Skipjack tuna	1.1-1.7 ng/g LW	Ueno *et al.* 2005	Offshore waters
East China Sea	Skipjack tuna	2.4-4.7 ng/g LW	Ueno *et al.* 2005	
Philippines	Skipjack tuna	2.1 ng/g LW	Ueno *et al.* 2005	Offshore waters
Brazil	Skipjack tuna	1.9 ng/g LW	Ueno *et al.* 2005	Offshore waters
Canada	Atlantic tomcod	77 ng/g LW	Law *et al.* 2003	
Chilika Lake, India	Irrawaddy dolphin	0.12-0.78 ng/g LW	Kannan *et al.* 2005	Endangered species
Hong Kong, China	Indo-Pacific humpback dolphin	33.6-720 ng/g LW	Ramu *et al.* 2005	Coastal waters 12% of ΣPBDEs
United Kingdom	White beaked dolphin	1480 ng/g LW	Law *et al.* 2003	Endangered species
Hong Kong, China	Finless porpoises	27.6-117.6 ng/g LW	Ramu *et al.* 2005	Coastal waters 12% of ΣPBDEs
Japan	Northern fur seal	2.64-4.56 ng/g LW	Kajiwara *et al.* 2004	Pacific coast 12% of ΣPBDEs

Svalbard, Arctic Norway	Polar bear	0.7-4.7 ng/g LW	Gabrielsen *et al.* 2004	
Canadian Arctic	Polar bear	1.04-11.3 ng/g LW	Muir *et al.* 2006	
Bjørnøya, Arctic Norway	Glacous gulls	0-7.9 ng/g LW	Herzke *et al.* 2003	
Norway	White-tailed sea eagle	6-184 ng/g LW	Herzke *et al.* 2005	In eggs. Endangered Species
Sweden	Peregrine falcons	110-9200 ng/g LW	Lindberg *et al.* 2004	Endangered species
Australia	Melon-headed whale	4.8 ng/g LW	Law *et al.* 2003	
Canada	Beluga whale	108 ng/g LW	Law *et al.* 2003	Vulnerable species
Netherlands	Mussels	0.3-11 ng/g LW	Law *et al.* 2003	Marine+freshwater
Sweden	Frog	5.6 ng/g LW	De Wit *et al.* 2004	
Canada	Zooplankton	0.46 ng/g LW	Law *et al.* 2003	

2.3.2 Trends

Most trend analysis show an increase in concentrations of PBDEs in the environment and in humans from the beginning of the 1970s, with a peak around the mid-1990s and a stabilisation or subsequent levelling off in Europe (Covaci *et al.* 2002, Fängström *et al.* 2005, Thomsen *et al.* 2005 and Knudsen *et al.* 2005), but with a continuous increase in the Arctic (Vorkamp *et al.* 2005, AMAP 2002 and AMAP 2005). PentaBDEs are reported in the studies to follow the same trend as ΣPBDEs. This increase has also been seen in North America, in air, soil and sediment, and wildlife, but insufficient data exist to allow comment on trends in the human population.

In the Asia-Pacific region a study on northern fur seals on the Pacific coast of Japan shows an increase of PBDEs to about 150 times between 1972 and 1994, and then levels decreased to about 50% in 1998 (Kajiwara *et al.* 2004). The reduction in PBDEs values was assumed to be due to the voluntary phase out of C-PentaBDE in Japan in 1990. BDE-99 levels showed the same pattern as ΣPBDEs.

Analysis of archived herring gull eggs (sampled in 1981, 1983, 1987, 1989, 1990, 1992, 1993, 1996, 1998, 1999 and 2000) enabled Norstrom *et al.* (2002) to establish temporal trends in PBDE concentrations over the period 1981-2000. At Lake Michigan, Lake Huron and Lake Ontario sampling sites, concentrations of tetra- and pentabromodiphenyl ethers (that is, BDE-47, BDE-99 and BDE-100) increased by 71-112-fold over these two decades (from 4.7 to 400.5 µg/kg ww at Lake Ontario; from 8.3 to 927.3 µg/kg ww at Lake Michigan; from 7.6 to 541.5 µg/kg ww at Lake Huron). These increases were found to be exponential at all three locations ($r^2 = 0.903 - 0.964$, $p < 0.00001$).

Wakeford *et al.* (2002) undertook sampling of eggs of the great blue heron in 1983, 1987, 1991, 1996, 1998 and 2000 in southern British Columbia and found that total PBDE concentrations (sum of tetra-, penta- and hexabromo-congeners) increased from 1.31 to 287 µg/kg ww between 1983 and 1996, but then dropped slightly to 193 µg/kg ww in 2000. They also undertook sampling of the eggs of thick billed murre in the Canadian North in 1975, 1987, 1993 and 1998, and observed a trend of gradually increasing PBDE concentrations (sum of tetra-, penta- and hexabromo-congeners) in these eggs from 0.43-0.89 µg/kg ww in 1975, to 1.83-3.06 µg/kg ww in 1998.

PBDEs have been detected in a variety of marine mammals. Alaee *et al.* (1999) reported average PBDE (di-to hexaBDE) concentrations in the blubber of marine mammals from the Canadian Arctic as 25.8 µg/kg lipid in female ringed seals (*Phoca hispida*), 50.0 µg/kg lipid in male ringed seals, 81.2 µg/kg lipid in female beluga (*Delphinapterus leucus*) and 160 µg/kg lipid in male beluga. BDE-47, a tetrabromodiphenyl ether, was the predominant congener, followed by the pentabromo BDE-99. Ikonomou *et al.* (2000, 2000b) reported PBDE concentrations in biota samples from the west coast and Northwest Territories of Canada. The highest concentration of of total PBDE residues, 2269 µg/kg lipid, was found in the blubber of a harbour porpoise form the Vancouver area. With a concentration of about

1200 µg/kg, one congener, BDE-47, accounted for slightly more than half of the total PBDE in the sample. Ikonomou *et al.* (2002a) analyzed temporal trends in Arctic marine mammals by measuring PBDE levels in the blubber of Arctic male ringed seals over the period 1981-2000. The mean total concentrations increased exponentially, from 0.572 µg/kg lipid in 1981 to 4.622 µg/kg in 2000, a greater than eightfold increase. They determined that Penta- and HexaBDEs are increasing at approximately the same rate (doubling time 4.7 and 4.3 years, respectively), more rapidly than TetraBDEs, for which the doubling time was 8.6 years. Once again, BDE-47 was predominant, followed by BDE-99 and BDE-100.

A marked increase in tissue PBDE levels was also evident in blubber samples collected from San Francisco Bay harbour seals over the period 1989 to 1998 (She *et al.* 2002). Total PBDEs (the sum of BDEs 47, 99, 100, 153 and 154) rose from 88 µg/kg lipid to a maximum of 8325 µg/kg lipid over this short period. Stern and Ikonomou (2000) examined PBDE levels in the blubber of make SE Baffin Bay beluga whales over the period 1982-1997, and found that the levels of total PBDEs (tri-to hexa-congeners) increased significantly, Mean total PBDE concentrations were about 2 µg/kg lipid in 1982, and reached a maximum value of about 15 µg/kg lipid in 1997. BDE-47 was the dominant congener, with a mean concentration of approximately 10 µg/kg lipid in 1997. Total PBDE residues (concentrations for individual congeners not provided) in the blubber of St Lawrence estuary belugas sampled in 1997-1999 amounted to 466 (±230) µg/kg ww blubber in adult males, and 655 (±457) µg/kg ww blubber in adult females. These values were approximately twenty times higher than concentrations in beluga samples collected in 1988-1990 (Lebeuf *et al.* 2001).

The results from a modelling exercise utilizing the European variant (EVn) BETR multimedia environmental fate model were presented for the C-PentaBDE product by Prevedouros *et al.* (2004). To predict future atmospheric concentration trends, the model was used in its fully dynamic mode over the period 1970-2010. It predicted that atmospheric concentrations would have peaked around 1997, and then declined with an overall "disappearance" half-life of 4.8 years. The model steady state simulations gave generally good agreement with measured data for BDE- 47 and BDE-99. The empirical data for North America presented above, however, show continuing increases in concentrations, at least up the year 2000, and so while the model results match some European data with fair agreement, they are not in accord with data from North America.

Three dated sediment cores from locations in Western Europe were analyzed for 14 BDE congeners (Zegers *et al.*, 2003). Cores from the Drammenfjord (Norway), the western Wadden Sea (The Netherlands) and Lake Woserin (Germany) showed a time dependent pattern in the distribution of BDEs since the start of production of PBDE formulations. Two of the three commercial formulations could be distinguished. The penta-mix formulation is clearly present from the beginning of the 1970s. This is in agreement with data for the industrial production of this formulation. In the cores from the Netherlands and Germany, concentrations of BDE congeners associated with the C-PentaBDE were levelling off in the most recent layers (1995 & 1997), whereas those in the Drammenfjord were still increasing in 1999. The absence of all BDE congeners in the older (deeper) layers of all three cores, as well as in several 100 to 150 million year old layers of clay from Kimmeridge, UK, indicated that these BDE congeners are not produced naturally.

Human exposure to polychlorobiphenyls and PBDEs in Japan in 1980 and 1995 showed that levels of the latter had increased substantially over the twenty-year period, although there was great variation between regions. The main congeners detected in serum were BDE-47 and BDE-99. Most total PBDE levels had more than doubled, and in one area increased twenty-fold, with 1995 values falling in the range 0.6 – 41.4 ng/g lipid Koizumi *et al.* 2006).

2.3.3. Bioavailability

Environmental studies on bioavailability have detected uptake of PentaBDE in soil organisms (Matscheko *et al.* 2002), sediment dwelling organisms (Magnusson *et al.* 2003) and aquatic organisms (Lithner *et al.* 2003, Voorspoels *et al.* 2003, Marsch *et al.* 2004, Kierkegaard *et al.* 2004, and Sinkkonen *et al.* 2004), making PentaBDE's way into the food webs evident. Subsequent bioaccumulation and biomagnification of the compound has been detected and described in Section 2.2.2.

Soil exposed to PBDEs in various ways was analyzed for BDE-47, BDE-66, BDE-99, BDE-100, BDE-153, BDE-154 and BDE-183 (Matscheko *et al.*, 2002). Earthworms collected at all soil sampling sites were analyzed as well. The BDE congener profile in all soil samples was dominated by BDE-47 and BDE-99. Accumulation of the compounds in earthworms from the sites yielded a direct relationship between the concentrations in the soil and concentrations in the worms. The biota-soil accumulation factors (BSAFs) of BDE congeners BDE-47, BDE-99 and BDE-100 were around 5 (organic matter/lipids). Thus, earthworms living in contaminated soils will accumulate tissue BDE concentrations and, as these animals represent the base of the terrestrial food chain for many organisms, this form a pathway for the accumulation of BDEs in organisms at higher trophic levels.

The western Scheldt estuary is subject to a variety of suspected PBDE sources, such as a brominated flame retardant manufacturing plant, Antwerp harbour, and the textile industry located further upstream. PBDE concentrations in samples of biota, including crab, shrimp, starfish, benthic fish (such as dab, goby, plaice and sole) and gadoid fish (such as bib and whiting) from the estuary were compared to those in samples from the Belgian North Sea beyond the mouth of the estuary (Voorspoels *et al.*, 2003). Eight BDE congeners (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, BDE-183 and BDE-209) were determined. Concentrations observed in the estuarine samples were up to 30 times higher than in those from the Belgian North Sea, with an increasing gradient towards Antwerp. Concentrations in the North Sea ranged from 0.02 to 1.5 μg/kg wet weight in benthic invertebrates and goby, from 0.06 to 0.94 μg/kg wet weight in fish muscle, and from 0.84 to 128 μg/kg wet weight in fish liver. The corresponding ranges in samples from the estuary were from 0.2 to 30, 0.08 to 6.9, and from 15 to 984 μg/kg wet weight, respectively. The ratio BDE-99/BDE-100 was found to be highly location- and species-dependent, possibly relating to differences in metabolism. In shrimp, the value of this ratio (4:1) was very similar to that observed in the Bromkal formulation and in estuarine sediment, and was similar in shrimp from both the North Sea and the estuary, implying both that these congeners are readily bioavailable and that shrimp lack the ability to metabolize either congener. On a lipid weight basis, concentrations of BDE-47 ranged from 3 to 108 μg/kg lipid weight in samples from the North Sea, and from 8 to 1,550 μg/kg lipid weight in estuarine samples. BDE-47 was the most abundant congener in all samples, comprising 43 to 75% of ΣBDE.

Thomas *et al.* (2004) conducted an input-output balance study of BDEs on three captive, juvenile grey seals. The animals were fed a diet of herring for six months, and the study was performed during the last three months of this period. BDE analysis was undertaken using GC-ECNIMS. Consistently high absorption (89 - 99%) was observed for all PBDE congeners studied (BDE-28, BDE-47, BDE-49, BDE-99, BDE-100, BDE-153, BDE-154 and BDE-209).

2.3.4 Human exposure

Studies, assessments and reviews referred to in this section have shown that the main routes for human exposure are food, and exposure to dust in indoor air at home and workplaces due to levels in products like furniture and electronic devices. Fish and agriculture products are the main food sources of PentaBDE for humans, and mother's milk for the nursing child. Fatty fish from contaminated areas are a major source (Sjödin *et al.* 2003). PentaBDE has been detected in various foods (VKM 2005, Burniston *et al.* 2003 and Bocio *et al.* 2003) as well as in indoor dust (Shoeib *et al.* 2004 and Wilford *et al.* 2005). Levels in foods in the US have been reported by Schecter *et al.* (2004), Schecter *et al* 2006, and Huwe *et al.* (2005). There are several hazard assessments in EU and US, looking into the exposure of humans

(VCCEP 2003, COT 2004, VKM 2005). They conclude that the available hazard or exposure information is inadequate to fully characterize the risks.

About 5% of the individuals in general populations have been found to be subjected to elevated exposure (Thomsen *et al.* 2005 b). This, together with estimates of the half life of C-PentaBDE congeners in humans, raises concern for long-term effects on human health. The half-lives for these congeners in humans have been estimated to be 1,040 days (BDE-99) and 573 days (BDE-100) (Geyer *et al.* 2004).

Domestic house dust is likely to be a significant source where furniture, carpet or appliances contain C-PentaBDE. This has been discussed in Section 2.1.1. It is not clear which sources are the greatest, and there could be wide variations depending on lifestyle and diet.

Several studies have detected levels of PentaBDE in sewage sludge (Matscheko *et al.* 2002, Fabrellas *et al.* 2004, Motche and Tanner 2004 and Sjödin *et al.* 2003, Hale 2002). Sewage sludge is considered to be one of the main sinks for PBDEs. The application of sewage sludge to agricultural land is one of the reasons for detected levels of PentaBDE in food products. This can explain the detected levels in vegetables and root crops in experimental studies. Levels in fish and root crops can be the source of exposure to domestic animals like chickens and pigs, and the source of PBDEs in meat products for human nourishment.

A Canadian global study showed that PentaBDE is widespread in human milk in populations all over the world (Ryan 2004). There are data on levels in human blood serum and milk from USA, Canada, Mexico, Japan, the EU region, the Arctic region and Scandinavia. A meta-analysis by Hites (2004), using data published up to mid-2003, showed that serum and milk levels in the US were much higher than those in Europe - ~35 ng/g *vs* ~ 2 ng/g lipid – and were doubling on average every 4-6 years. BDE-47 and BDE-99 were the major congeners detected. Considerably higher levels are found in humans from North America in general. About 5% of general populations have been found to be subjected to elevated exposure. Thus, together with estimates of the half-life of PentaBDE congeners in humans, raiss concern for long-term effects on human health (Thomsen *et al.* 2005b).

Levels increasing from the 1980s to the 2000s have been observed in mother's milk from Sweden as well as in blood from Germany and Norway (Sjödin *et al.* 2003). A more recent study in Sweden (Fängström *et al.* 2005) assessed the temporal trends of polybrominated diphenyl ethers (PBDEs), in mothers' milk in the Stockholm area. The pooled samples were covering the time period 1980 to 2004, with emphasis on samples from the last ten years. Concentrations of BDE-47, BDE-99 and BDE-100 reached a peak in the mid-1990s and are now clearly showing decreasing levels. The concentrations are however still much higher than in 1980.

The objective of a recent Norwegian study was to complete and extend a previous study on time trends of PBDEs in Norwegian pooled serum samples (Thomsen *et al.* 2005a) and put together an overview of the PBDE body burden in the general population from 1977 to 2004. The temporal trend of the sum of seven PBDEs (BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154 and BDE-183) in the pooled serum from the present study are in close agreement with the levels found in a previous study by the same authors. In general, for similar time periods the levels in breast milk seem to be somewhat lower than in the serum, but the same overall trend is observed. This confirms that the PBDE body burdens in these regions have risen rapidly from 1977 to about 1997, but now seem to have stabilized or even to have decreased. This is in accordance with the trends observed in Swedish breast milk, as an indicator of the European situation, but may not be true of levels in North America. The PBDE level was previously found to be about twice as high in a serum pool from infants up to four years of age compared to serum pools from elderly persons. This finding was confirmed in the Norwegian study. However, in 2002, children between the ages of 5 and 14 years showed higher levels of PBDEs than the average adult.

Contemporary PBDE concentrations in Europe and Asia are remarkably similar, with low median values on a lipid basis for all countries and relatively small variations. The situation in North America is completely different with median values for individual studies in the range of 20-50 ng/g LW (Ryan 2004). However, in parallel with the regional differences that were reported above for biota, the levels in breast adipose tissue taken from women living in San Francisco Bay area in 2000 were almost two orders of magnitude higher than what has been reported in human milk from Sweden (Sjödin *et al.* 2003). A more recent study of levels in human adipose tissue in New York was published by Johnson-Restrepo *et al.* (2005). The study of 40 males and 12 females of a range of ages and ethnicities showed wide variations in lipid PBDE concentrations, with mean values substantially higher than the medians. Median concentrations were: BDE-47, 29.3 ng/g lipid; BDE-99, 10.3 ng/g lipid; BDE-100, 12.0 ng/g lipid.

In a preliminary screening of PBDEs in plasma and milk samples from Mexican women, the levels were well above European levels of PBDEs reported so far (López *et al.* 2004). The mean level of PBDEs (with BDE-209 excluded) in Mexican women living in urban areas was approx. 20 ng/g LW in plasma. The levels in women living in rural areas in Mexico were however comparable with women living in rural areas in Sweden. (BDE-209 levels were only detected in women living in the Mexican city).

Ryan (2004) detected a big individual variation in levels in the general population in a study from Canada. The values span more than three orders of magnitude, with a few values showing a much greater level. Levels detected in the Canadian Arctic in Ryan's study (2004) were increasing. Values in human milk from the Faroe Islands showed the same trend (Fängström *et al.* 2004).

Two studies in Australia indicated that levels of PBDEs in Australian breast milk and blood serum are higher than those in Europe but lower than those found in North America (Harden *et al.* 2004 and 2005).

*Table 2.6 Data on mean levels of PentaBDE (**BDE-99**) (ng/g LW) in humans from different parts of the world.*

Data	**Country/region**	**Levels**	**References**	**Year**	**Comments**
blood	The Netherlands	0.8	Weiss *et al.* 2004	unknown	
blood	Norway	1.0	Thomsen *et al.* 2004	1999	
blood	Mexico	2.0	López *et al.* 2004	2003	Urban population
blood	Australia	2.3	Harden *et al.* 2004	2003	
milk	Germany	0.2	Harden *et al.* 2004	2000	
milk	Sweden	0.3	Fängström *et al.* 2005	2003	Urban population
milk	Mexico	0.6	López *et al.* 2004	2003	Rural population
milk	Sweden	0.5	López *et al.* 2004	2003	Rural population
milk	United Kingdom	0.9	Harden *et al.* 2004	?	median
milk	Faroe Islands	1.0	Fängström *et al.* 2004	1999	Rural population
milk	Australia	1.9	Harden et al. 2005	2002/2003	
milk	Canada	4	Ryan *et al.* 2002	2002	Rural population
milk	USA	28	Päpke *et al.* 2001	2000	Urban population

Although they are less relevant that environmental data, results from occupational studies bear out the facility with which the PBDEs are taken up by human bodies. In Sweden, occupational exposure to PBDE has been identified among electronics recycling personnel (Sjødin *et al.*, 1999) and in technicians responsible for repair and maintenance of computers (Jacobsson *et al.*, 2002) as well as in nearby soil and sediment (Wang *et al.* 2005). Also workers in industry manufacturing C-PentaBDE, or polyurethane foam and electronic equipment containing it can be exposed to PentaBDE. There is an extensive literature on such exposures.

2.3.5 Debromination

There is growing interest in the fate of PBDEs in the environment. In experiments reported by Stapleton *et al.* (2004), carp were fed food spiked with individual BDE congeners for 62 days, and tissue and excreta were examined. At least 9.5±0.8% of BDE-99 in the gut was reductively debrominated to BDE-47 (one less bromine) and assimilated in carp tissues. Similarly, 17% of the heptabromo congener BDE-183 was reductively debrominated to hexabromo congeners. The authors noted that body burdens of PBDEs may thus reflect direct uptake from exposure as well as debromination of more highly brominated congeners. Highly selective reductive microbial debrominations were observed in experiments reported by He *et al.* (2006). Hepta- and Octa-BDEs were produced in cultures of *Sulfurospirillum multivorans* to which DecaBDE had been added, but OctaBDE was not attacked in a similar system. Cultures of an alternative organism, *Dehalococcoides sp.*, failed to attack the DecaBDE but an OctaDBE mixture was extensively changed, yielding a mixture of Hepta- through Di-BDEs which included the PentaBDE, BDE-99. The authors draw attention to the potential for conversion of higher congeners in the environment to more toxic congeners with fewer bromine substituents. Further studies particularly environmental monitoring studies focussing on congeners for which the primary source is likely to be debromination reactions, are required to clarify the role of debromination in determining the final mix of PBDE congeners in the environment.

Hydroxylated BDEs (OH-BDEs) have been detected and identified as metabolites in several species after exposure to specific BDE congeners but have also been found to occur as natural products in marine sponges and ascidians (Marsch *et al.* 2004). Methoxylated BDEs (MeO-BDEs) have also been reported as natural products present in marine sponges and green algae. It would seem that the origin of these substances can be natural, anthropogenic or both. Nine OH-BDEs and six MeO-BDEs were identified in blood of Baltic Sea salmon (*Salmo salar*) using newly synthesized standards (Marsch *et al.*, 2004). All of the identified OH- and MeO-BDEs were substituted with four or five bromine atoms and five of them also had one chlorine substituent. Fourteen have the methoxy or hydroxy group substituted in the position *ortho*-to the diphenyl ether bond. The structures of several of the compounds support natural rather than anthropogenic origins. However, at least one of the OH-BDEs (4'-OH-BDE-49) may be a hydroxylated metabolite of BDE-47. Estrogenic activity of some hydroxylated PBDEs has been reported by Meerts *et al.* (2001).

Other studies of metabolism of PBDEs are summarized in Section 2.2.2.1.

2.4 Hazard assessment for endpoints of concern

Evidence to date suggests that the major congeners of the C-PentaBDE formulation, BDE-47 and BDE-99, are likely to be more toxic and bioaccumulative than other PBDE congeners. Although the toxicology of PBDEs is not completely understood, some studies on PentaBDE have demonstrated reproductive toxicity, neurodevelopmental toxicity and effects on thyroid hormones. The neurotoxic effects of PBDEs are similar to those observed for PCBs and so children exposed to PBDEs are likely to be prone to subtle but measurable developmental problems. It is presumed that PBDEs are endocrine disrupters, but research results in this area are scant (Siddiqi *et al.* 2003).

While further studies follow internationally-accepted guidelines might be needed to make a full risk assessment of the situations of children, there are sufficient data for development of the present risk profile.

It is acknowledged that these conclusions rest to some extent on examination of reviews, rather than reanalysis of primary data, but in general the studies under review have followed internationally accepted experimental protocols. Nonetheless, there is no significant disagreement between some reported results and later analyses, such as that of the US Voluntary Children's Chemical Evaluation Program (VCCEP) (2005).

2.4.1 Ecotoxicity

Recent studies show that exposure to BDE-47 can cause growth inhibition in colonies of the plankton algae (*Skeletonema costatum*) and a depression on reproductive output of the zooplankton *Daphnia magna* (Källqvist *et al.* 2006).

A recent paper by Timme-Laragy *et al.* (2006) showed adverse effects on fish development at low concentrations. However, the endpoints that were affected in this report (behavioural learning) are not usually accepted risk assessment endpoints. Other endpoints that would be acceptable, such as growth or survival, were not affected.

Canada was able to perform a risk quotient analysis for each congener, integrating known or potential exposures with known or potential adverse effects. In its simplest form, the risk quotient may be described by the equation:

$$\text{Risk quotient} = \frac{\text{exposure reference value}}{\text{toxicity reference value}}$$

and it is customary to use conservative values in order to highlight the worst case.

Exposures were estimated local to emission sources including areas receiving urban drainage (wildlife consumers) and downstream of a polymer processing facility (benthic organisms). Adjustment factots of 100-1000-fold were applied to critical toxicity values to reflect extrapolation from laboratory to fielod conditions, intraspecies and interspecies variations in sensitivity, and because compounds are bioaccumulative and persistent.

A risk quotient value >1 signifies the likelihood or potential for adverse effects to occur, while those <1 imply no danger to organisms. The Canadian results shown in Table 3.1 are based partly on Canadian empirical data and partly on surrogate data from Swedish and US sources.

Table 3.1 Risk quotient values for PentaBDE (Environment Canada 2006, Canadian Wildlife Table 8).

Commercial Product	**Pelagic organisms**	**Benthic organisms**	**Soil organisms**	**Wildlife consumers**
C-PentaBDE	4x10^{-3}	45.2	0.13-0.26	149

These values reflect the bioaccumulation of PentaBDE which causes organisms higher in the food chain to be exposed to greater risk.

2.4.2 Effects in mammals

In a review article on toxic effects of brominated flame retardants, Darnerud (2003) drew on a range of primary literature to conclude that exposure to PBDEs gives rise to adverse effects in experimental *in vivo* models, and depending on type of product different effects are seen, occurring at varying dose levels. Generally, the C-PentaBDE products cause effects at the lower dosages. The critical effects of PentaBDE are those on neurobehavioral development and, although somewhat less sensitive, thyroid hormones in offspring (from 0.6 to 0.8 and 6 to 10 mg/kg body wt., respectively) (Darnerud 2003). Note that some data reported in Table 2.7 show levels below these. More recent information, especially for North America, is available in Birnbaum and Staskal (2004).

Blubber biopsy and blood samples were collected from weaned grey seal (*Halichoerus grypus*) pups and juveniles during 1998 and 1999 (Hall *et al.*, 2003). Fifty four post-weaned pups and fifty five first year juveniles (of which thirteen were recaptured post- weaned pups) were studied. The median concentrations of ΣBDE (14 congeners) were 0.17 and 0.46 μg/kg lipid weight in the blubber of the pups and the juveniles, respectively. The study indicated that thyroid hormone levels in the blood of grey seals during their first year of life were significantly, and positively, related to ΣBDE concentrations in blubber, after accounting for the effects of possible confounding variables. Such an association is not, in itself, sufficient evidence for a causal relationship, but is in accordance with the hypothesis that these compounds can act as endocrine disrupters in grey seal pups.

Darnerud (2003) concluded in his review that for PentaBDEs, the critical effects among the available studies seem to be developmental neurotoxicity and, although generally at somewhat higher doses, altered thyroid hormone homeostasis. Regarding the neurotoxicity in mice, no clear mechanism could be defined but effects of the PentaBDEs both via thyroid hormone disruption and directly on signal transmission in brain have been discussed. For example, a number of PBDEs were capable of inducing cell death of cerebellar granule cells in culture (Reistad *et al.*, 2002, Reistad and Mariussen 2005). The LOAEL value for PentaBDE could be set to 0.6–0.8 mg/kg body wt., based on the most sensitive effect observed, neurobehavioral effects during early development (Darnerud 2003, although it is not the task of the POPRC to set a regulatory level, for construction of which resort would need to be made a wider range of data.

In a hazard assessment by the Committee on Food Safety in Norway (VKM 2005) the following toxic effects of exposure to BDE-99 or the C-PentaBDE formulation was reported: neurotoxicity, effects on neurobehavioral development, effects on the thyroid hormone system and hispatological alterations in the tyroid and liver.

Table 2.7 Overview of No Observed Effect level (NOEL) and Lowest Observed Effect Level (LOEL) after oral administration of ***BDE-99*** *congener or C-PentaBDE formulations. Bold values are the lowest LOEL or NOEL detected.**

PentaBDE	**Duration**	**Dose**	**NOEL mg/kg/ day**	**LOEL mg/kg/day**	**Endpoint**	**Species**	**Reference**
BDE-99	s.d	0.8 or 12.0 mg/kg	n.d.	0.8	Neurotoxicity Behaviour, motor activity level and learning	mouse	Eriksson *et al.* 2001
BDE-99	s.d	0.6, 6, or 30 mg/kg	n.d.	0.6	Developmental- and neurotoxicity Behaviour - hypoactive	mouse	Branchi *et al.* 2002
BDE-99	s.d	0.4, 0.8, 4.0, 8.0, or 16 mg/kg	**0.4**	**0.8**	Developmental- and neurotoxicity Behaviour	mouse	Viberg *et al.* 2004 Sand *et al.* 2004
BDE-99	s.d.	0,06 and 0,3 mg/kg to pregnant female	**n.d.**	**0,06**	Developmental- and neurotoxicity Behaviour (increased activity)	rat, F1 gen.	Kuriyama *et al.* 2005
BDE-99	s.d.	0,06 and 0,3 mg/kg to pregnant female	**0,06**	**0,3**	Reduced testis size and number of sperms	rat, F1 gen.	Kuriyama *et al.* 2005

Penta mix DE-71	30 d	0.01, 0.05, 0.1, 0.5, or 1.0 mg/kg/day	1	n.d.	Growth, food intake, hematology, histopatology Clinical chemistry	rat	Great lakes Chemical Corporation 1985
Penta mix DE-71	30 d	0, 3, 30, or 60 mg/kg/day	3	30	Liver weight, puberty, reproduction, liver enzymes, T_4-reduction	Male rat	Stoker *et al.* 2004
Penta mix DE-71	30 d	0, 3, 30, or 60 mg/kg/day	n.d.	3	T_4-reduction	Female rat	Stoker *et al.* 2004
Penta mix DE-71	35 d	0, 1, 10 or 30 mg/kg/day	1	10	T_4-reduction Liver enzymes	pregnant rat	Zhou *et al.* 2002, Zhou *et al.* 2001
Penta mix DE-71	90 d	0-0.44 mg/kg/day	n.d.	0.44	Liver enzymes	rat	Carlson 1980
Penta mix DE-71	90 d	0, 2,10, or 100 mg/kg/day	0-2	2-10	Hepatocyto-megali Tyreoidea hyperplasi	rat	Great lakes Chemical Corporation 1984

n.d. = not defined, s.d. = single dose

* Most of the studies are in line with the OECD test guidelines and for those are not, the quality of the study is assessed to be adequate.

The PBDE mixture known as DE-71 (71% bromine by mass, and containing BDE-47, BDE-99, BDE-100, BDE-153, BDE-154) delays the puberty and suppresses the growth of androgen-dependent tissues in male Wistar rat following a peri-pubertal exposure. These effects suggest that DE-71 may be either inducing steroid hormone metabolism or acting as an androgen receptor (AR) antagonist (Stoker *et al.* 2005).

Talsness *et al.* (2005) evaluated the effects of environmentally relevant concentrations (low doses) of BDE-99 on the female reproductive system in rats. Ultra structural changes compatible with altered mitochondrial morphology were observed in the ovaries of the F1 offspring. No statistically significant changes in ovarian follicle counts were observed. External and skeletal anomalies were detected in offspring (F2) from two different dams (F1) with early developmental exposure to 300 µg BDE-99/Ikg BW. Exposure to BDE-99 resulted in female reproductive tract changes in the F1 generation which were apparent at adulthood.

In utero exposure to a single low dose of BDE-99 disrupts neurobehavioral development and causes permanent effects on the rat male reproductive system apparent in adulthood (Kuriyama *et al.* 2005). Also in this study, the effects of developmental exposure to BDE-99 on juvenile basal motor activity levels and adult male reproductive health were assessed. The exposure to low-dose BDE-99 during development caused hyperactivity in the offspring at both time points (postnatal days 36 and 71) and permanently impaired spermatogenesis by the means of reduced sperm and spermatid counts. The doses used in this study of 60 and 300 µg/kg BW are relevant to human exposure levels, being approximately 6 and 29 times, respectively, higher than the highest level reported in human breast adipose tissue. This is the lowest dose of PBDE reported to date to have an *in vivo* toxic effect in rodents and supports the premise that low-dose studies should be encouraged for hazard identification of persistent environmental pollutants. The study by Viberg *et al.* (2004) shows that neonatal exposure to BDE-99 can induce developmental neurotoxic effects, such as changes in spontaneous behaviour (hyperactivity), effects that are dose-response related and worsen with age. The changes are seen in C57/B1 mice of both sexes. Spontaneous behaviour (locomotion, rearing, and total activity) was observed in two-, five- and eight-month-old mice.

2.4.3 Toxicity to humans

Several hazard assessments have been produced in EU and in US. The conclusions in the hazard assessments elaborated are qualified by the lack of sufficient knowledge of the toxicology of PentaBDE to enable assessment of the risk to humans (COT 2004, VKM 2005 and VCCEP 2003). The toxicological importance for humans of detected effects in laboratory animals is not clear. There is still not enough knowledge of the mechanisms, half-life and metabolism of PentaBDE in experimental animals and humans (VKM 2005).

The conclusion in the hazard assessment by the Committee on Food Safety in Norway was that the exposure through food and mother's milk is considerably lower than the observed NOEL in laboratory mammals (VKM 2005). It is believed that long-time exposure to lower doses of PentaBDE can cause health effects, since PentaBDE accumulates in the human body. Since the half-life of PentaBDE in humans is not known it is not possible today to conclude on long-time exposure effects. This is true even for the US situation, where levels may be 10-20 times those observed in Europe, but pharmacokinetics, toxicology, exposure and other critical data are lacking.

Vulnerable groups could however be pregnant women, embryos and infants, because of effects on the thyroid hormone balance, and the embryo's development of the central nervous system. During pregnancy, maintenance of the thyroid hormone balance is a physiological challenge. Embryos and infants are particularly vulnerable for reductions in thyroid hormone levels (VKM 2005). Infants are exposed to PentaBDE through the diets of their mothers' milk, since PentaBDE is lipophilic and accumulates in the milk (VKM 2005).

3. Synthesis of information

3.1 Summary

PentaBDE meets all of the Annex D screening criteria, and details are included (for the sake of completeness) in Table 3.2, below.

In the absence of production controls, the levels detected in humans, other species and the environment have been observed to rise steeply and this increase is observed in remote locations as well as closer to sites of production and use. In the US, where C-PentaBDE was in high use until recently and where it remains in such materials as polyurethane foam incorporated into consumer products, there has been a build-up in human tissue.

PentaBDE in soil or sediment is readily incorporated into the food chain and bioaccumulates in the fatty tissues of top predators, including humans.

There are toxicological studies of concern that demonstrate neurodevelopmental impacts in animals at low tissue levels that are of relevance to levels observed in populations. Such body burdens remain under close review.

An assessment of the impact of PBDEs on the environment was recently concluded by Environment Canada (2006), taking into account critical studies and lines of evidence that support the conclusion that these commercial substances entering the environment have or may have an immediate or long-term harmful effect on the environment or its biodiversity.

4. Concluding statement

Pentabromodiphenyl ether (C-PentaBDE) is a synthetic mixture of anthropogenic origin with no known natural occurrence. It can be concluded therefore that the presence of components of PFOS in the environment is the result of anthropogenic activities. Long range transport must be responsible for its presence in areas such as the Arctic region, remote from sites of production and release. PentaBDE degrades slowly in the environmernt and can bioaccumulate and biomagnify in mammals and piscivorous birds.

The phase out of C-PentaBDE production and use has led to a reduction in current use but many materials in use, such as polyurethane foams and plastics in electronic equipment, contain PentaBDE which is slowly released to the environment. This release will be accelerated at end-of-life of such materials, especially during recovery and recycling operations.

Although levels of PentaBDE in human blood and milk, and in other environmental species, are falling in Europe, they continue to increase in North America and the Arctic region.

Based on the information in this risk profile, C-PentaBDE, due to the characteristics of its components, is likely, as a result of long-range environmental transport and demonstrated toxicity in a range of non-human species, to cause significant adverse effects on human health and the environment, such that global action is warranted.

References:

Agrell, C., ter Schure, A.F.H., Sveder, J., Bokenstrand, A., Larsson, P. and Zegers, B.N. 2004. Polybrominated diphenyl ethers (PBDEs) at a solid waste incineration plant. I: atmospheric concentrations. Atmos. Environ. 38: 5139-3148.

Alaee, M., Luross, M.J., Whittle, M.D. and Sergeant D.B. 2002. Bioaccumulation of polybrominated diphenyl ethers in the Lake Ontario pelagic food web. Organohalogen Compounds 57: 427-430.

Alaee, M., Arias, P., Sjödin, A. and Bergman, Å. 2003. An overview of commercially used brominated flame retardants, their applications, their use patterns in different countries/regions and possible modes of releases. Env. Int. 29: 683-689.

AMAP Assessment 2002: Persistent organic pollutants in the Arctic. Arctic monitoring and assessment program, Oslo 2004.

AMAP 2005. Fact sheet: Brominated flame retardants in the Arctic. http://www.amap.no

Ballschmiter, K., Mennel, A. and Buyten, J. 1993. Long-chain Alkyl Polysiloxanes as Non-Polar Stationary Phases in Capillary Gas Chromatography, Fresenius' J. Anal. Chem. 346: 396-402.

Birnbaum, L., Staskal, D.F. and Diliberto, J.J. 2003. Health effects of polybrominated dibenzo-*p*-dioxins (PBDDs) and dibenzofurans (PBDFs). Environ. Int. 29: 855-860.

Birnbaum, L. And Staskal, D.F. 2004. Brominated flame retardants: cause for concern? Environ. Health Perspectives. 112: 9-17.

Bocio, A., Llobet, J.M., Domingo, J.L., Corbella, J., Teixidó, A. and Casas C. 2003. J. Agric. Polybrominated Diphenyl Ethers (PBDEs) in Foodstuffs: Human Exposure through the Diet. Food Chem. 51: 3191 - 3195; (Article) DOI: 10.1021/jf0340916

Branchi, I., Alleva, E. and Costa, L.G. 2002. Effects of perinatal exposure to a polybrominated diphenyl ether (PBDE-99) on mouse neurobehavioral development. Neurotoxicology 23:375-84.

Broman, D., Balk, L., Zebühr, Y. and Warman K. 2001. Miljöövervakning i Stockholmskommun Saltsjön och Mälaren . KEMI Slutrapport: Provtagningsåren 96/97, 97/98 och 98/99. Laboratoriet för akvatisk ekotoxikologi, ITM, Stockholms universitet samt Miljölaboratoriet i Nyköping.

BSEF, Brominated Science and Environmental Forum. 2001. Major brominated flame retardants volume estimates. Total market demand by region 2001. 21 January 2003. www.bsef.com.

BSEF 2006. Information provided by the BSEF in July 2006. Figures for 2004 and 2005 will be forthcoming.

Burniston, D.A., Symons, R.K., Croft, M., Trout, M. and Korth, W. 2003. Determination of polybrominated diphenyl ethers (PBDEs) in Australian pig fat. Organohalogen Compounds, Volumes 60-65 (Dioxin 2003) Boston, MA.

Burreau, S., Broman, D. and Zebühr Y. 1999. Biomagnification quantification of PBDEs in fish using stable nitrogen isotopes. Organohalogen Compdounds 40: 363 - 366.

Burreau, S., Zebühr, Y., Ishaq, R. and Broman D., 2000. Comparison of biomagnification of PBDEs in food chains from the Baltic Sea and the Northern Atlantic Sea. Organohalogen Compdounds 47: 253-255.

Burreau, S., Zebühr, Y., Broman, D. and Ishaq, R. 2004. Biomagnification of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) studies in pike (*Esox lucius*), perch (*Perca fluviatilis*) and roach (*Rutilus rutilus*) from the Baltic Sea. Chemosphere 55: 1043-1052.

Butt, C.M., Diamond, M.L., Truong, J., Ikonomou, M.G. and ter Schure, A. 2004. A Spatial Distribution of Polybrominated Diphenyl Ethers in Southern Ontario as Measured in Indoor and Outdoor Window Organic Films. Environ. Sci. Technol. 38: 724-731.

Carlson, G.P. 1980. Induction of xenobiotic metabolism in rats by brominated diphenyl ethers administered for 90 days. Toxicol. Lett. 6:207-12.

Christensen, J.H., Glasius, M., Pécseli, M., Platz, J. and Pritzl, G. 2002. Polybrominated diphenyl ethers (PBDEs) in marine fish and blue mussels from southern Greenland. Chemosphere 47: 631-638.

CITI. 2000. The bioaccumulation of compound S512 by carp. Chemical Biotesting Center, Chemicals Inspection and Testing Institute, Tokyo. As cited in: Risk Assessment of Diphenyl Ether, Pentabromoderivative, Commission of the European Communities, 2000.

Committee on toxicity of chemicals in food consumer products and the environment. COT statement on brominated flame retardants in fish from Skerne-Tees rivers system. 2004. http://www.food.gov.k/multimedia/pdfs/bfrstatement.pdf

Covaci, A., Gheorghe, A., Steen Redeker, E., Blust, R. and Schepens, P. 2002a. Distribution of organochlorine and organobromine pollutants in two sediment cores from the Scheldt estuary (Belgium). Organohalogen Compounds 57: 239-242.

Covaci, A., Van de Vijver, K., DeCoen, W., Das, K., Bouqeugneau, J.M., Blust, R. and Schepens, P. 2002b. Determination of organohalogenated contaminants in liver of harbour porpoises (*Phocoena phocoena*) stranded on the Belgian North Sea coast. Mar. Pollut. Bull. 44: 1157-1165.

Danish EPA. 1999. Brominated flame retardants. Substance flow analysis and assessment of alternatives.

Darnerud, P.O. 2003. Toxic effects of brominated flame retardants in man and wildlife. Environ. Int. 29: 841-853.

Darnerud, P.O., Aune, M., Atuma, S., Becker, W., Bjerselius, R., Cnattingius, S. and Glynn, A. 2002. Time trend of polybrominated diphenyl ether (PBDE) levels in breast milk from Uppsala, Sweden, 1996-2001. Organohalogen Compd. 58: 233-236.

de Wit, C., Alaee, M. and Muir, D. 2004. Brominated flame retardants in the Arctic – an overview of spatial and temporal trends. Organohalogen Compounds 66: 3764-3769.

D'Silva, K., Thompson, H., Fernandes, A. and Duff, M. 2004. PBDEs in Heron Adipose Tissue and Eggs from the United Kingdom. Abstract. BFR 2004.

Ebert, J. and Bahadir, M. 2003. Formation of PBDD/F from flame retarded plastic materials under thermal stress. Environ. Int. 29: 711-716.

EMEP. 2004. New substances: Model assessment of potential for long-range transboundary atmospheric transport and persistence of PentaBDE. EMEP contribution to the preparatory work for the review of the CLRTAP protocol on POPs. Information note 10/2004.

Environment Canada. 2006. Ecological Screening Assessment Report on Polybrominated Diphenyl Ethers (PBDEs). January 2006.

Eriksson, P., Jakobsson, E. and Fredriksson, A. 2001. Brominated flame retardants: a novel class of developmental neurotoxicants in our environment? Environmental Health Perspectives 109: 903-8.

EU. 2000. Risk Assessment of Diphenyl Ether, Pentabromoderivative (Pentabromodiphenyl Ether). CAS Number: 32534-81-9, EINECS Number: 251-084-2. Final Report of August 2000, Commission of the European Communities. Rapporteur: United Kingdom.

Fabrellas, B., Larrazabal, D., Martinez, M.A., Eljarrat, E. andBarceló, D. 2004. Presence of polybrominated diphenyl ethers in Spanish sewage sludges: important contribution of deca-BDE. Organohalogen Compounds. 66: 3755-3760.

Fängström, B., Strid, A., Athanassiadis, I., Grandjean, P., Wiehe, P. and Bergman Å. 2004. A retrospective study of PBDEs in human milk from the Faroe Islands. The third international workshop on brominated flame retardants, BFR 2004.

Fängström, B., Strid, A. and Bergman, Å. 2005. Rapport til Naturvårdsverket för prosjektet ”Analys av polybromerade difenyletrar (PBDE) och hexabromcyklododekan (HBCDD) i human mjölk från Stockholm – en tidstrend studie. (Dnr 721-2653-05Mm) Stockholm 2005-11-23.

Fjeld E., Mariussen, M., Strand-Andersen, M., Hjerpset, M. og Schlabach M. 2003. Bioakkumulering og fordeling av polybromerte difenyletere i norske innsjøer. NFRs program for forurensninger: kilder, spredning, effekter og tiltak (ProFO). Foredrag, forskerseminar 15. okt. 2003, Olavsgård hotell.

Fjeld, E., Schlabach, M., Berge, J.A., Eggen, T., Snilsberg, P., Källberg, G., Rognerud, S., Enge, E.K., Borgen, A. and Gundersen, H. 2004. Kartlegging av utvalgte nye organiske miljøgifter – bromerte flammehemmere, klorerte parafiner, bisfenol A og triclosan (Screening of selected new organic contaminants – brominated flame retardants, chlorinated paraffins, bisphenol-A and triclosan). NIVA-rapport 4809-2004, Oslo. (SFT: TA-2006). 106 sider.

Fjeld, E. et al. 2005. Screening of selected new organic contaminants 2004. Brominated flame retrardants, perflourated alkylated substances, irgarol, diuron, BHT and dicofol. NIVA-report 5011-2005, Oslo, pp. 97.

Fredonia Group. 2005. Specialty Plastic Additives to 2009. Study # 1961. Available for a fee from www.fredonia.ecnext.com (accessed July 2006).

Gabrielsen, G.W., Knudsen, L.B., Verreault, J., Push, K., Muir, D.C. and Letcher, J. 2004. Halogenated organic contaminants and metabolites in blood and adipose tissues of polar bears (*Ursus maritimus*) from Svalbard. SFT-report 915/2004. www.sft.no

Geyer, H. J., Schramm, K.W., Darnerud, P.O., Aune, M., Henkelmann, B., Lenoir, D., Schmid, P. and McDonald, T.A., 2004. Terminal elimination half-lives of the brominated flame retardants TBBPA, HBCD and lower brominated PBDEs in humans. Organohalogen compounds 66:3820-3825.

Gouin, T., Thomas, G.O., Cousins, I., Barber, J., Mackay, D. and Jones, K.C. 2002. Air-Surface Exchange of Polybrominated Diphenyl Ethers and Polychlorobiphenyls. Environ. Sci. Technol. 36: 1426-1434.

Gouin, T. and Harner, T. 2003. Modelling the Environmental Fate of the PBDEs. Environment International. 29:717-724.

Great Lakes Chemical Corporation (1984). 90-day dietary study in rats with pentabromodiphenyl oxide (DE-71). Final report. 1984. Report No.: Project No. WIL-12011,WIL Research Laboratories, Inc.

Hale, R.C., La Guardia, M.J., Harvey, E.P. and Mainor, M. 2002. Potential role of fireretardant-treated polyurethane foam as a source of brominated diphenyl ethers to the US environment. Chemosphere. 46: 729-735.

Hall, A.J., Kalantzi, O.I. and Thomas, G.O. 2003. Polybrominated diphenyl ethers (PBDEs) in grey seals during their first year of life – are they thyroid hormone endocrine disrupters ? Environmental Pollution 126: 29-37.

Harden, F.A, Toms, L.M.L, Ryan, J.J. and Mueller, J. F. 2004. Determination of the levels of polybrominated diphenylethers (PBDEs) in pooled blood sera obtained from Australians aged 31-45 years. In: Proceedings of the Third International Workshop on Brominated Flame Retardants, June 6-9 2004, Toronto, Canada: 59-62

Harden, F., Müller, J. and Toms, L. 2005, Organochlorine Pesticides (OCPs) and Polybrominated Diphenyl Ethers (PBDEs) in the Australian Population: Levels in Human Milk, Environment Protection and Heritage Council of Australia and New Zealand http://www.ephc.gov.au/pdf/EPHC/OCP_PBDE_human_milk_jan%202005.pdf

Harner, T., Ikonomou, M., Shoeib, M., Stern, G. and Diamond, M. 2002. Passive air sampling results for polybrominated diphenyl ethers along an urban-rural transect. 4th Annual Workshop on Brominated Flame Retardants in the Environment, June 17-18, Canada centre for Inland Waters, Burlington, Ontario, pp. 51-54.

Harrad, S. and Hunter, S. 2004. Spatial Variation in Atmospheric Levels of PBDEs in Passive Air Samples on an Urban-Rural Transect. Organohalogen Compounds. 66: 3786-3792.

Harrad, S., Wijesekara, R., Hunter, S., Halliwell, C. and Baker, R. 2004. Preliminary Assessment of UK Human Dietary and Inhalation Exposure to Polybrominated Diphenyl Ethers. Environ. Sci. Technol. 38: 2345-2350.

Hassanin, A., Breivik, K., Meijer, S.N., Steinnes, E., Thomas, G.O. and Jones, K.C. 2004. PBDEs in European Background Soils: Levels and Factors Controlling Their Distribution. Environ. Sci. Technol. 38: 738-745.

Hayakawa K, Takatsuki H, Watanabe I. and Sakai S. 2004. Polybrominated diphenyl ethers (PBDEs), polybrominated dibenzo-p-dioxins/dibenzofurans (PBDD/Fs) and monobromo-polychlorinated dibenzofurans (MoBPXDD/Fs) in the atmosphere and bulk deposition in Kyoto, Japan. Chemosphere 57: 343-356.

He, J., Robrock, K.R. and Alvarez-Cohen, L. 2006. Microbial Reductive Debromination of Polybrominated Diphenyl Ethers (PBDEs). Environ. Sci. Technol. 40: 4429-4434.

Herzke, D., Gabrielsen, G.W., Evenset, A. and Burkow, I.C. 2003. Polychlorinated camphenes (toxaphenes), polybrominated diphenylethers and other halogenated organic pollutants in Glaucous Gull (*Ularus hyperboreus*) from Svalbard and Bjørnøya (Bear Island). Environmental Pollution 121: 293-300.

Herzke, D., Berger, U., Kallenborn, R., Nygård, T. and Vetter, W. 2005. Brominated flame retardants and other organobromines in Norwegian predatory bird eggs. Chemosphere 61: 441-449.

Hites, R.A. 2004. Polybrominated Diphenyl Ethers in the Environment and in People: A Meta-Analysis of Concentrations. Environ. Sci. Technol. 38: 945-956.

Hoh, E. and Hites, R.A. 2005. Brominated Flame Retardants in the Atmosphere of the East-Central United States. Environ. Sci. Technol. 39: 7794-7802.

Huwe, J.K. and Larsen, G.L. 2005. Polychlorinated Dioxins, Furans, and Biphenyls, and Polybrominated Diphenyl Ethers in a U.DS. Meat Market Basket and Estimates of Dietary Intake. Environ. Sci. Technol. 39: 5606-5611.

Ikonomou, M.G., Raine, S. and Adisson, R.F. 2002. Exponential Increases of the Brominated Flame Retardants Polybrominated Diphenyl Ethers, in the Canadian Arctic From 1981-2000. Environ. Sci. Technol. 36: 1886-1892.

International Environment Reporter. 2006. Material available for a fee – see www.bna.com.

Jakobsson, K. Thuresson, K., Rylander, L., Sjödin, A., Hagnar, L. and Bergman, A. 2002. Exposure to polybrominated diphenyl ethers and tetrabromobisphenol A among computer technicians. Chemosphere 46: 709-716.

Jaspers, V., Covaci, A., Maervoet, J., Dauwe, T., Schepens, P. ands, M. 2004. Brominated flame retardants in Belgian little owl (*Athene noctua*) eggs. Organohalogen Compounds 66: 3856-3860.

Jaward, F.M., Farrar, N.J., Harner, T., Sweetman, A.J. and Jones, K.C. 2004. Passive Aair Ssampling of PCBs, PBDEs, and Organochlorine Pesticides Across Europe. Environ. Sci. Technol. 38: 34-41.

Johnson-Restrepo, B., Kannan, K., Rapaport, D.P., and Rodan, B.D. 2005. Polybrominated Diphenyl Ethers and Polychlorinated Biphenyls in Human Adipose Tissue from New York. Environ. Sci. Technol. 39: 5177-5182.

Kajiwara, N., Ueno, D., Takahashi, A., Baba, N. and Tanabe, S. 2004. Polybrominated Diphenyl Ethers and Organochlorines in Archived Northern Fur Seals Samples From The Pacific Coast of Japan, 1972-1998. Environ. Sci. Technol. 38: 3804-3809.

Kannan, K., Ramu, K., Kajiwara, N., Sinha, R.K. and Tanabe, S. 2005. Organochlorine pesticides, polychlorinated biphenyls, and polybrominated diphenyl ethers in Irrawaddy dolphins from India. Arch. Environ. Contamination 49: 415-420.

Källqvist, T., Grung, M. and Tollefsen, K-E. Chronic toxicity of 2,4,2',4'-tetrabromodiphenyl ether (BDE-47) on the marine alga *Skeletonema costatum* and the crustacean *Daphnia magna*. Environmental Toxicology and Chemistry (accepted for publication).

Kierkegaard, A., Bignert, A., Sellström, U., Olsson, M., Asplund, L., Jansson, B. and de Wit, C.A. 2004a. Polybrominated diphenyl ethers (PBDEs) and their methoxylated derivatives in pike from Swedish waters with emphasis on temporal trends, 1967-2000. Environmental Pollution 130: 187-198.

Knudsen, L. B., Gabrielse, G. W., Verreault, J., Barrett, R., Skåre, J.U., Polder, A. and Lie, E. 2005. Temporal trends of brominated flame retardants, cyclododeca-1,5,9-triene and mercury in eggs of four seabird species from Northern Norway and Svalbard. SFT-report 942/2005.

Koizumi, A., Yoshinaga, T., Harada, K., Inoue, K., Morikawa, A., Muroi, J., Inoue, S., Eslami, B., Fujii, S., Fujimine, Y., Hachiya, N., Koda, S., Kusaka, Y., Murata, K., Nakatsuka, N., Omae, K., Saito, N., Shimbo, S., Takenaka, K., Takeshita, T., Todoriki, H., Wada, Y., Watanabe, T. and Ikeda, M. 2006. Assessment of human exposure to polychlorinated biphenyls and polybrominated diphenyl ethers in Japan using archived samples from thee arly 1980s and mid-1990s. Environmental Res. Accepted for publication December 2004, still 'in press' when accessed at www.elsevier.com/locate/envres in June 2006.

Kuriyama, S.N., Talsness, C.E., Grote, K. and Chahoud, I. 2005 Developmental exposure to low dose PBDE-99: effects on male fertility and neurobehavior in rat offspring. Environmental Health Perspectives 113(2):149-54.

Law, R. J., Alaee, M., Allchin, C.R., Boon, J.P., Lebeuf, M., Lepom, P. and Stern, G.A. 2003. Levels and trends of polybrominated diphenylethers and brominated flame retardants in wildlife. Environment International 29: 757-770.

Law, R.J., Allchin, C.R., de Boer, J., Covaci, A., Herzke, D., Lepom, P., Morris, S., Tronczynski, J. and de Wit, C.A. 2005. Levels and Trends of Brominated Flame Retardants in European and Greenland Environments. Chemosphere 64: 187-208.

Lee, R.G.M., Thomas, G.O. and Jones, K.C. 2004. PBDEs in the Atmosphere of Western Europe. Environ. Sci. Technol. 38: 699-706.

Lindberg, P., Sellström, U., Häggberg, L. and de Wit, C.A. 2004. Higher Brominated Diphenyl Ethers and Hexabromocyclododecane Found in Eggs of Peregrine Falcons (*Falco peregrinus*) Breeding in Sweden. Environ. Sci. Technol. 38: 93-96.

Lithner, G., Holm, K. and Ekström, C. 2003. Metaller och organiska miljögifter i vattenlevande organismer och deras miljö i Stockholm 2001. ITM Rapport 108, 87 pp., Institute of Applied Environmental Research (ITM), Stockholm University, Stockholm, Sweden, ISBN 91-631-3758-5 (in Swedish).

López, D., Athanasiadou, M. and Athanassiadis, I. 2004. A preliminary study on PBDEs and HBCD in blood and milk from Mexican women. The third international workshop on brominated flame retardants, BFR 2004.

Magnusson, K., Agrenius, S. and Ekelund, R. 2003. Distribution of a tetrabrominated diphenyl ether and its metabolites in soft-bottom sediment and macrofauna species. Mar. Ecol. Prog. Ser. 255: 155-170.

Marsch, G., Athanasiadou, M., Bergman, Å. and Asplund, L. 2004. Identification of Hydroxylated and Methoxylated Polybrominated Diphenyl Ethers in Baltic Sea salmon (*Salmo salar*) Blood. Environ. Sci. Technol. 38: 10-18.

Matcheko, N., Tysklind, M., de Wit, C., Bergek, S., Andersson, R. and Sellström, U. 2002. Application of sewage sludge to arable land – soil concentrations of polybrominated diphenyl ethers and polychlorinated dibenzo-p-dioxins, dibenzofurans, and biphenyls, and their accumulation in earth worms. Environ. Toxicol. Chem. 21: 2515-2525.

Meerts, I.A., Letcher, R.J., Hoving, S., Marsh, G., Bergman, A., Lemmen, J.G., van der Burg, B. and Brouwer, A. 2001. *In vitro* estrogenicity of polybrominated diphenyl ethers, hydroxylated PBDEs, and polybrominated bisphenol A compounds. Environ. Health Perspect. 109(4): 399-407.

Moche, W. and Thanner, G. 2004. Levels of PBDE in effluents and sludge from sewage treatment plants in Austria. Proceedings of the Third International Workshop on Brominated Flame Retardants BFR2004, Toronto, Canada, June 6-9 2004. pp. 167-170.

Morf, L.S., Tremp, J., Huber, Y., Stengele, M. and Zenegg, M. 2005. Brominated flame retardants in waste electrical and electronic equipment: substance flow in a recycling plant. Environ. Sci. Technol. 39: 8691-8699.

Muir, D.C.G., Backus, S., Derocher, A.E., Dietz, R., Evans, T.J., Gabrielsen, G.W., Nagy, J., Norström, R.J., Sonne, C., Stirling, I., Taylor, M.K. and Letcher, R. J. 2006. Brominated flame retardants in polar bears (Ursus maritimus) from Alaska, the Canadian Arctic, East Greenland, and Svalbard. Environ. Sci. Technol. 40: 449-455.

Norström, R.J., Simon, M., Moisey, J., Wakeford, B. and Weseloh, D.V.C. 2002. Geographical Distribution (2000) and Temporal Trends (1981-2000) of Brominated Diphenyl Ethers and Hexabromocyclododecane in Guillemot Eggs from Baltic Sea. Environ. Sci. Technol. 37: 5496-5501.

Nylund, K., Asplund, L., Jansson, B., Jonsson, P., Litzén, K. and Sellström, U. 1992. Analysis of some polyhalogenated organic pollutants in sediments and sewage sludge. Chemosphere, 24: 1721-1730.

Päpke, O., Bergman, Å., Fürst, P., Meironyté, G.D., and Herrmann, T. 2001. Determination of PBDEs in human milk from the United States - comparison of results from three laboratories. Organohalogen Compounds. 52: 197-200.

Palm, A. 2001. The Environmental Fate of Polybrominated Diphenyl Ethers in the centre of Stockholm – Assessment of Using a Multimedia Fugacity Model. Master of Science Thesis, Umeå Universitat.

Palm, A., Cousins, I.T., Mackay, D., Tysklind, M., Metcalf, C. and Alaee, M. 2002. Assessing the Environmental Fate of Chemicals of Emerging Concern: A Case Study of the PBDEs. Environ. Poll. 117: 195-213.

Peltola, J. and Yla-Mononen, L. 2001. Pentabromodiphenyl ether as a global POP. TemaNord 2001, vol. 579. Copenhagen: Nordic Council of Ministres; ISBN 92-893-0690-4: 78 pp.

Prevedouros, K., Jones, K.C. and Sweetman, A.J. 2004a. European-Scale Modelling of Concentrations and Distribution of Polybrominated Diphenyl Ethers in the Pentabromodiphenyl Ether Product. Environ. Sci. Technol. 38: 5993-6001.

Prevedouros, K., Jones, K.C. and Sweetman, A.J. 2004b. Estimation of the Production, Consumption, and Atmospheric Emissions of Pentabrominated Diphenyl Ethers in Europe Between 1970 and 2000. Environ. Sci. Technol. 38: 3224-3231.

Ramu, K., Kajiwara, N., Tanabe, S., Lam, P.K.S. and Jefferson, T.A. 2005. Polybrominated diphenyl ethers (PBDEs) and organochlorines in small cetaceans from Hong Kong waters: Levels, profiles and distribution. Marine Poll. Bull. 51: 669-676.

Reistad, T., Mariussen, E. and Fonnum, F. 2002. The effects of polybrominated flame retardants on cell death and free radical formation in cerebellar granule cells. Organohalogen Compd 57: 391-394.

Reistad, T. and Mariussen, E. 2005. A commercial mixture of the brominated flame retardant pentabrominated diphenyl ether (DE-71) induces respiratory burst in human neutrophil granulocytes *in vitro*. Toxicol. Sci. 87: 57-65.

Ryan, J.J., Patry, B., Mills, P. and Beaudoin G. 2002. Recent trends in levels of brominated diphenyl ethers (BDEs) in human milks from Canada. Organohalogen Compounds. 58: 173-176.

Ryan, J.J. 2004. Polybrominated diphenyl ethers (PBDEs) in human milk; occurrence worldwide. The third international workshop on brominated flame retardants, BFR 2004.

Sand, S., von Rosen, D., Eriksson, P., Fredriksson, A., Viberg, H., Victorin, K. and Filipsson, A.F. 2004. Dose-response modeling and benchmark calculations from spontaneous behaviour data on mice neonatally exposed to 2,2',4,4',5-pentabromodiphenyl ether. Toxicol. Sci. 81: 491-501.

Schecter, A., Päpke, O., Tung, K-C., Staskal, D. and Birnbaum, L. 2004. Polybrominated Diphenyl Ethers Contamination of United States Food. Environ. Sci. Technol. 38: 5306-5311.

Schecter, A., Päpke, O., Harris, T.R., Tung, K-C., Musumba, A., Olson, J. and Birnbaum, L. 2006. Polybrominated Diphenyl Ether (PBDE) Levels in an Expanded market basket Survey of United States (US) Food and Estimated PBDE Intake by Age and Gender. Environ. Health. Perspectives. Doi:10.1289/ehp.9121 (prepublication viewed online 13 July 2006).

ter Schure, A.F.H. and Larsson, P. 2002. Polybrominated diphenyl ethers in precipitation in Southern Sweden (Skåne, Lund). Atmos. Environ. 36: 4015-4022.

ter Schure, A.F.H., Larsson, P., Agrell, C., and Boon, J.P. 2004a. Atmospheric Transport of Polybrominated Diphenyl Ethers and Polychlorinated Biphenyls to the Baltic Sea. Environ. Sci. Technol. 38: 1282-1287.

ter Schure, A.F.H., Agrell, C., Bokenstrand, A., Sveder, J., Larsson, P. and Zegers, B.N. 2004b. Polybrominated diphenyl ethers at a solid waste incineration plant. II: atmospheric deposition. Atmos. Environ. 38: 5149-5155.

Sellström, U. 1996. PBDEs in the Swedish environment. Licentiate Thesis, Institute of Applied Research, Stockholm University.

Sellström, U., Bignert, A., Kierkegaard, A., Häggberg, L., de Wit, C.A., Olsson, M. and Jansson, B. 2003. Temporal Trend Studies on Tetra- and Pentabrominated Diphenyl Ethers and Hexabromocyclododecane in Guillemot Eggs From the Baltic Sea. Environ. Sci. Technol. 37: 5496-5501.

Shoeib, M., Harner, T., Ikonomou, M. and Kannan, K. 2004. Indoor and Outdoor Concentrations and Phase Partitioning of Perfluoroalkyl Sulfonamides and Polybrominated Diphenyl Ethers. Environ. Sci. Technol. 38: 1313-1320.

Siddiqi, M.A., Laessig, R.H. and Reed, K.D. 2003. Polybrominated diphenyl ethers (PBDEs): new pollutants – old diseases. Clin Med Res. 1(4):281-90.

Sinkkonen, S., Rantalainen, A.-L., Paasivirta, J. and Lahtiperä, M. 2004. Polybrominated methoxy diphenyl ethers (MeO-PBDEs) in fish and guillemot of Baltic, Atlantic and Arctic environments. Chemosphere 56: 767-775.

Sjödin, A., Patterson, D.G. and Bergman Å. 2003. A review on human exposure to brominated flame retardants – particularly polybrominated diphenyl ethers. Environ. Int. 29: 829-839.

Sjödin, A., Hagmar, L., Klasson-Wehler, E., Kronholm-Diab, K., Jakobsson, E. and Bergman, A. 1999. Flame retardant exposure: polybrominated diphenyl ethers in blood from Swedish workers. Environ. Health perspectives 107: 643-648.

Stapleton, H.M., Letcher, R.J. and Baker, J.E. 2004. Debrominated Diphenyl Ether Congeners BDE 99 and BDE 183 in the Intestinal Tract of the Common Carp (*Cyprinus carpio*). Environ. Sci. Technol. 38: 1054-1061.

Stapleton, H.M., Dodder, N.G., Offenberg, J.H., Schantz, M.M. and Wise, S.A. 2005. Polybrominated Diphenyl Ethers in House Dust and Clothes Dryer Lint. Environ. Sci. Technol. 39: 925-931.

Stoker, T.E., Laws, S.C., Crofton, K.M., Hedge, J.M., Ferrell, J.M. and Cooper, R.L. 2004. Assessment of DE-71, a commercial polybrominated diphenyl ether (PBDE) mixture, in the EDSP male and female pubertal protocols. Toxicol Sci. 78(1): 144-55.

Stoker, T.E., Cooper, R.L., Lambright, C.S., Wilson, V.S., Furr, J. and Gray, L.E. 2005. *In vivo* and *in vitro* anti-androgenic effects of DE-71, a commercial polybrominated diphenyl ether (PBDE) mixture. Toxicol. Appl. Pharmacol. 207(1): 78-88.

Strandberg, B., Dodder, N.G., Basu, I. and Hites, R.A. 2001. Concentrations and Spatial Variations of Polybrominated Diphenyl Ethers and Other Organohalogen Compounds in Great Lakes Air. Environ. Sci. Technol. 35: 1078-1083.

Swiss Agency for the Environment. 2002. Environmentally hazardous substances: Selected polybrominated flame retardants, PBDE and TBBPA – Substance flow analysis. Environmental series No. 338.

Sørmo, E.G., Salmer, M.P., Jenssen, B.M., Hop, H., Bæk, K., Kovacs, K.M., Lydersen, C., Falk-Pettersen, S., Gabrielsen, G.W., Lie, E. and Skaare, J.U. 2006. Biomagnification of brominated flame retardants in the polar bear food chain in Svalbard, Norway. Accepted for publication in Environmental Toxicology and Chemistry.

Talsness, C.E., Shakibaei, M., Kuriyama, S.N., Grande, S.W., Sterner-Kock, A., Schnitker, P., de Souza, C., Grote, K. and Chahoud, I. 2005. Ultrastructural changes observed in rat ovaries following *in utero* and lactational exposure to low doses of a polybrominated flame retardant. Toxicol. Lett. 157(3):189-202.

Thomas, G.O., Moss, S.E.W., Asplund, L. and Hall, A.J. 2005. Absorption of decabromodiphenyl ether and other organohalogen chemicals by grey seals (*Halichoerus grypus*). Environ. Pollut. 133: 581-6.

Thomsen, C., Frøshaug, M., Becher, G., Kvalem, H.E, Knutsen, H., Alexander, J., Bergsten, C. and Meltzer, H.M. 2004. PBDEs in serum from persons with varying consumption of fish and game. The third international workshop on brominated flame retardants, BFR 2004.

Thomsen, C., Liane, V., Frøshaug, M. and Becher, G. 2005a. Levels of brominated flame retardants in human samples from Norway through three decades. Organohalogen Compounds. 67: 658-661.

Thomsen, C., Frøshaug, M., Broadwell, S.L.,Becher, G. and Eggesbø, M. 2005b. Levels of brominated flame retardants in milk from the Norwegian Human Milk Study: HUMIS. Organohalogen Compounds. 67: 509-512.

Thron, K.U., Bruhn, R. and McLachlan, M.S. 2004. The influence of age, sex, body-condition, and region on the levels of PBDEs and toxaphene in harbour porpoises from European waters. Fresenius Environ. Bull. 13: 146-155.

Timme-Laragy, A.R., Levin, E.D. and Di Giulio, R.T. 2006. Developmental and behavioural effects of embryonic exposure to the polybrominated diphenyl ether mixture DE-71 in the killfish (*Fundulus heteroclitus*). Chemosphere 62: 1097-1104.

Ueno, D., Kajiwara, N., Tanaka, H., Subramanian, A., Fillmann, G., Lam, P.K.S., Zheng, G.J., Muchitar, M., Razak, H., Prudente, M., Chung, K. and Tanabe, S. 2004. Global Pollution Monitoring of Polybrominated Diphenyl Ethers Using Skipjack Tuna as a Bioindicator. Environ. Sci. Technol. 38: 2312-2316.

Van der Goon, D., van het Bolscher, M., Visschedijk, A.J.H. and Zandveld, P.Y.J. 2005. Study to the effectiveness of the UNECE persistent organic pollutants protocol and cost of possible additional measures. Phase I: Estimation of emission reduction resulting from the implementation of the POP protocol. TNO-report 2005/194.

VCCEP. 2003. US Voluntary Children's Chemical Evaluation Program. 2003. Tier 1 Assessment of the Potential Health Risks to Children Associated With Exposure to the Commercial Pentabromodiphenyl Ether Product, prepared for Great Lakes Chemical Corporation.

VCCEP. 2005. US Voluntary Children's Chemical Evaluation Program (VCCEP), Summary of Tier 1 Hazard Assessment, document 25 August 2005, accessed July 2006. http://www.epa.gov.chemrtk/vccep/pubs/finalpenoct.pdf.

Verreault, J., Gabrielsen, G.W., Letcher, R.I., Muir, D.C.G., and Chu, S. 2004. New and established organohalogen contaminants and their metabolites in plasma and eggs of glaucous gulls from Bear Island. SPFO-Report: 914/2004.

Verreault, J., Gabrielsen, G.W., Chu, S., Muir, D.C.G., Andersen, M., Hamaed, A. and Letcher, R.I.. 2005. Flame Retardants and Methoxylated and Hydroxylated Polybrominated Diphenyl Ethers in Two Norwegian Arctic Top Predators: Glaucous Gulls and Polar Bears. Environ. Sci. Technol. 39: 6021-6028.

Viberg, H., Fredriksson, A. and Eriksson, P. 2002. Neonatal exposure to the brominated flame retardant 2,2',4,4',5-pentabromodiphenyl ether causes altered susceptibility in the cholinergic transmitter system in the adult mouse. Toxicol. Sci. 67: 104-7

Viberg, H., Fredriksson, A. and Eriksson, P. 2004. Investigation of strain and/or gender differences in developmental neurotoxic effects of polybrominated diphenyl ethers in mice. Toxicol. Sci. 81: 344-53.

VKM 2005. Vitenskapskomiteen for mattrygghet (Norwegian Scientific Committee for food safety.) Utalelse fra faggruppen for forurensninger, naturlige toksiner og medisinrester i matkjeden. Risikovurdering av PBDE. 04/504.

Vives, I., Grimalt, J.O., Lacorte, S., Guillamón, M., Barceló, D. and Rosseland, B.O. 2004. Polybromodiphenyl Ether Flame Retardants in Fish from Lakes in European High Mountains and Greenland. Environ. Sci. Technol. 38: 2338-2344.

Voorspoels, S., Covaci, A. and Schepens, P. 2003. Polybrominated Diphenyl Ethers in Marine Species from the Belgian North Sea and the Western Scheldt Estuary: Levels, Profiles and Distribution. Environ. Sci. Technol. 37: 4348-4357.

Vorkamp, K., Christensen, J.H., Glasius, M. and Riget, F.R. 2004a. Persistent halogenated compounds in black guillemots (*Cepphus grylle*) from Greenland – levels, compound patterns and spatial trends. Mar. Pollut. Bull. 48: 111-121.

Vorkamp, K., Christensen, J.H. and Riget, F.R. 2004b. Polybrominated diphenyl ethers and organochlorine compounds in biota from the marine environment of East Greenland. Sci. Total Environ. 331: 143-155.

Vorkamp, K., Thomsen, M., Falk, K., Leslie, H., Møller, S. and Sørensen, P.B. 2005. Temporal Development of Brominated Flame Retardants in Peregrine Falcon *(Falco peregrinus)* Eggs from South Greenland (1986-2003). Environ. Sci. Technol 39: 8199-8206.

Vulykh, N., Dutchak, S., Mantseva, E. and Shatalov, V. 2004. EMEP contribution to the preparatory work for the review of the CLRTAP protocol on persistent organic pollutants. New Substances: Model assessment of potential for lon-range transboundary atmospheric transport and persistence of PentaBDE. EMEP MSC-E Information Note 10/2004. Metrological Synthesizing Centre-East.

Wang, D., Cai, Z., Jiang, G., Leung, A., Wong, M.H. and Wong, W.K. 2005. Determination of polybrominated diphenylethers in soil and sediment from an electronic waste recycling facility. Chemosphere 60: 810-816.

Washington State Polybrominated Diphenyl Ether (PBDE) Chemical Action Plan: Draft Final Plan, December 1, 2005.

Weber, R. and Kuch, B. 2003. relevance of BFRs and thermal conditions on the formation pathways of brominated and brominated-chlorinated dibenzodioxins and dibenzofurans. Environ. Int. 29: 699-710.

Weiss, J., Meijer, L., Sauer, P., Lindeholm, L., Athanasiadis, I. and Bergman, Å. 2004. PBDE and HBCDD levels in blood from Dutch mothers and infants. The third international workshop on brominated flame retardants, BFR 2004.

Wilford, B.H., Shoeib, M., Harner, T., Zhu, J. and Jones, K.C. 2005. Polybrominated Diphenyl Ethers in Indoor Dust in Ottawa, Canada: Implications for Sources and Exposure. Environ. Sci. Technol. 39(18): 7027-7035.

Wolkers, H., van Bavel, B., Derocher, A.E., Wiig, Ø., Kovacs, K.M., Lydersen, C. and Lindström, G. 2004. Congener-Specific Accumulation and Food Chain Transfer of Polybrominated Diphenyl Ethers in Two Arctic Food Chains. Environ. Sci. Technol. 38: 1667-1674.

Xin-Ming Wang, Ding, X., Mai, B-X., Xie, Z-Q., Xiang, C-H., Sun, L-G., Sheng, G-Y., Fu, J-M. and Zeng, E.Y. 2005. Polybrominated Diphenyl Ethers in Airborne Particulates Collected During a Research Expedition from the Bohair Sea to the Arctic. Environ. Sci. Technol. 39: 7803-7809.

Zegers, B.N., Lewis, W.E. and Boon, J.P. 2000. Levels of Some Polybrominated Diphenyl Ether (PBDE) Flame Retardants in Dated Sediment Cores. Organohalogen Compounds, 47: 229-232.

Zegers, B.N., Lewis, W.A., Booij, K., Smittenberg, R.H., Boer, W., de Boer, J. and Boon, J.P. 2003. Levels of polybrominated diphenyl ether flame retardants in sediment cores from Western Europe. Environ. Sci. Technol. 37: 3803-3807.

Zennegg, M., Kohler, M., Gerecke, A.C. and Schmid, P. 2003. Polybrominated diphenyl ethers in whitefish from Swiss lakes and farmed rainbow trout. Chemosphere 51: 545-553.

Zhou, T., Ross, D.G., DeVito, M.J.and Crofton, K.M. 2001. Effects of short-term in vivo exposure to polybrominated diphenyl ethers on thyroid hormones and hepatic enzyme activities in weanling rats. Toxicol. Sci. 61: 76-82.

Zhou, T., Taylor, M.M., De Vito, M.J. and Crofton, K.M. 2002. Developmental exposure to brominated diphenyl ethers results in thyroid hormone disruption. Toxicol. Sci. 66: 105-1 16.

別添9

商業用オクタブロモジフェニルエーテルの危険性の概要

分解性	蓄積性	人健康影響	動植物への影響
【生分解性】 分解せず（OECD TG 301D） 【半減期】 ・大気中：（Hexa-Nona BDE）30.4-161.0日（OH ﾗｼﾞｶﾙとの反応）（AOPWIN）	【BCF（経鰓的生物濃縮係数）】 ・ｺｲ：（HexaBDPE）BCF=2580-5640 ・ｺｲ：（HeptaBDE）BCF＜1.1-3.8 ・ｺｲ：（OctaBDE）BCF＜9.5 ・ｺｲ：（c-OctaBDE）BCF）＜10-36 【BMF（経口的生物濃縮係数）】 ・飼育中のﾀｲｾｲﾖｳｻｹの餌に含まれるHeptaBDE 183 をﾓﾆﾀｰした結果、95%がｻｹに蓄積。 【BSAF（生物相-底質濃縮係数）】 ・2 種の淡水魚：（HexaBDE）BSAF =1，（HeptaBDE）BSAF =2 ・（BDE 154） BSAF =9.1±1.1	【反復投与毒性】 ラット（28 日）：10mg/kg/day で T4 濃度減少（octa-BDE:30.7%, hepta-BDE:45.1%,） 【催奇形性・発生毒性】 ウサギ（経口 妊娠 7～19 日）：5mg/kg/day で胎児毒性、15mg/kg/day で児の肝重量増加、体重増加量減少、骨形成遅延 マウス（生後 10 日目単回）：0.45mg/kg で 2、4 及び 6 月齢での異常行動並びに成長後の空間認識能・記憶の影響（BDE153）	アメリカチョウゲンボウ *Falco sparverius* ：18.7μg PBDEs/egg 及び15.6±0.3 ng PBDEs/g bw/dayで29日間曝露した雛鳥において、PHA応答（T細胞媒介性免疫）が増大し、抗体媒介性反応が減少した。脾臓（胚中心の減少）、滑液嚢（アポトーシスの減少）、胸腺（マクロファージの増大）に構造的変化あり。脾臓の体細胞指標とPBDEs間及び滑液嚢の体細胞指標とBDE-47間に負の相関性あり。

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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 commercial octabromodiphenyl ether

At its third meeting, the Persistent Organic Pollutants Review Committee adopted the risk profile on commercial octabromodiphenyl ether, on the basis of the draft contained in document UNEP/POPS/POPRC.3/14. The text of the risk profile, as amended, is set out below. It has not been formally edited.

COMMERCIAL OCTABROMODIPHENYL ETHER

RISK PROFILE

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

November 2007

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Executive summary

The European Union and its Member States, which are Parties to the Stockholm Convention, submitted a proposal in July 2006 for listing octabromodiphenyl ether in Annex A of the Stockholm Convention pursuant to paragraph 1 of Article 8 of the Convention, and the POPRC agreed that the commercial product Commercial octabromodiphenyl ether (c-OctaBDE) – actually a mixture as described below - met the screening criteria of Annex D to the Convention. This risk profile reviews the available information on the commercial mixture and its main components: Hexa, Hepta, Octa and NonaBDE.

The polybrominated diphenyl ethers in general are used as flame retardants of the additive type. They are physically combined with the material being treated rather than chemically combined (as in reactive flame retardants). The commercial products cover several congeners and bromination levels. The information provided by the bromine industry indicates that (c-OctaBDE) has been produced in The Netherlands, France, USA, Japan, UK and Israel, but since 2004, it is no longer produced in the EU, USA and the Pacific Rim and there is no information that indicates it is being produced in developing countries. According to the Bromine Science and Environmental Forum (BSEF), OctaBDE was commercialized sometime in the mid 70's. By the early 2000's global production was <4000 tonnes/year and by the time production ceased, demand was <500 tonnes; assuming 30 years of production at 6000 tonnes per year total production volume would be around 180,000 tonnes.

Although the commercial OctaBDE seems to be not longer produced, releases during the service life of articles containing the commercial mixtures and at the end of article service life during disposal operations are still relevant. Switzerland reported for this country diffuse emission from the use of products containing OctaBDE of about 0.37 t/a (based on worst-case estimations) for a total stock of 680 tons.

The persistence of c-OctaBDE components in the environment is well documented. The only relevant degradation pathways identified until now are photolysis, anaerobic degradation and metabolism in biota, acting through debromination and producing other BDE which may have higher toxicity and bioaccumulation potential.

Assessing the bioaccumulation potential of c-OctaBDE components constitutes a main challenge in this risk profile. A high potential for bioaccumulation (including a moderate potential for bioconcentration) and food-web biomagnification has been demonstrated for HexaBDE; and it is fully in line with the reported elimination rates. The food-web biomagnification has been reported for HeptaBDE, although at a lower extend than expected from the Kow; this fact can be explained by metabolism resulting in a relatively short half-life (experimentally demonstrated and explained by the authors by debromination). The presence of Octa and NonaBDE in biota is well document but its potential for bioaccumulation from water and food is much lower than expected from their Kow. Reduced availability, metabolisms or both can justify this fact. The number of scientific papers demonstrating debromination of Octa to DecaBDE to other PBDEs is continuously increasing; this is critical for the assessment as would indicate that the supposed low bioaccumulation potential could be in reality the consequence of metabolism to bioaccumulative PBDEs. A quantitative estimation cannot be presented yet, but the debromination process has been already reported for aquatic organisms, mammals and birds. This is an active research field, and new results will need to be assessed by the POPRC as they appear in refereed literature.

Biota monitoring data in remote areas offer the best demonstration on the potential for long range transport of the c-OctaBDE components, Hexa and HeptaBDE. The role of atmospheric transport is confirmed based on its detection in alpine lakes. The potential for long range transport has been observed for DecaBDE. The lack of confirmation for Octa and NonaBDE may be related to the lower relative contribution and/or metabolism via debromination.

No relevant effects have been observed in aquatic, sediment and soil laboratory studies; however, the measured endpoints and the exposure conditions employed in these assays are clearly insufficient for a proper assessment of chemicals such as Hexa to NonaBDE.

The available information on mammals and birds offer relevant information. The lowest reported NOAEL for traditional endpoints is 2-5 mg/kg bw/d. The effects are relevant for the health and the ecological assessments and therefore useful for assessing risks for humans and wildlife. In addition, immuno-toxicological effects and particularly delayed neurotoxic effects observed after a single dose require specific attention. A critical body burden for HexaBDE 153 of 2000 µg/kg lipid has been estimated based on a NOEL of 0.45 mg/kg; it should be noted that HexaBDE 153 concentrations close to these value have been found in several species and geographic sites and total PBDE concentrations frequently exceed this threshold by a large margin.

The evaluation of the human and environmental risk of commercial OctaBDE associated to its potential for long range transport must consider that the commercial product is a mixture of components with different properties and profiles, which may also be released to the environment due to its presence as components of other PBDE commercial products and also produced in the environment by debromination of commercial DecaBDE.

The greatest difficulty appears for the estimation of the potential hazard of the commercial mixture and its components. There are traditional ecotoxicological and toxicological studies where no effects have been observed even at unrealistically high concentrations. However, an in-depth assessment of these studies considering in particular the properties and toxicokinetic of PBDE indicates that the test design, exposure conditions and measured endpoints are not appropriate for a sound assessment of these types of chemicals. Thus, the lack of effects reported in those tests should be considered with care. Specific studies have reported particular hazards such as delayed neurotoxicity and immunotoxicity which may be particularly relevant in the assessment of both human health and ecosystem risks; although a quantitative evaluation of these effects in terms of hazard for human health and ecosystem is not possible based on the current level of information, it may become feasible soon if additional scientifically sound information is produced at a similar rate than in recent years.

Based on the existing evidence, it is concluded that the Hexa and HeptaBDE components of the octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

The increasing evidence related to debromination of Octa and Nona BDE into BDEs with POPs properties and considering that under Article 8, paragraph 7(a) of the Convention states that the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the Octa and NonaBDE components of the octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

1. Introduction

The Stockholm Convention is a global treaty to protect human health and the environment from persistent organic pollutants (POPs), of which twelve are currently listed under the Convention. POPs are chemicals that remain intact in the environment for long periods, become widely distributed geographically, accumulate in living organisms and can cause harm to humans and the environment. The European Union and its Member States, which are Parties to the Stockholm Convention, submitted a proposal in July 2006 for listing octabromodiphenyl ether in Annex A of the Stockholm Convention pursuant to paragraph 1 of Article 8 of the Convention, and the POPRC agreed that the commercial product Commercial octabromodiphenyl ether – actually a mixture as described below - met the screening criteria of Annex D to the Convention.

1.1 Chemical identity of the proposed substance

This proposal concerns the c-OctaBDE. There are several components in the commercial product, with different properties and potential risks. Thus this risk profile focuses on the assessment of individual components of the commercial product, and the final compilation for an overall assessment of the commercial product itself.

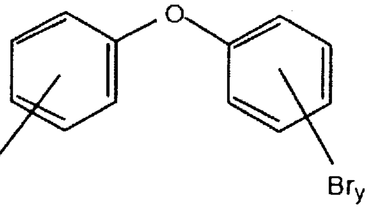
It is believed that little if any c-OctaBDE is produced since the major supplier located in North America stopped production in 2004. The commercially supplied OctaBDE was complex mixture consisting (as of 2001 within the EU Member States) typically of ≤0.5% Pentabromodiphenyl ether isomers, ≤12% Hexabromodiphenyl ether isomers, ≤45% Heptabromodiphenyl ether isomers, ≤33% OctaBDE isomers, ≤10% Nonabromodiphenyl ether isomers and ≤0.7% Decabromodiphenyl ether. The composition of older products or products from non-EU countries may be different from this.

The c-OctaBDE is sold as a technical grade under the Chemical Abstracts Service (CAS) Registry number for the OctaBDE isomer.

IUPAC Name: Diphenyl ether, octabromo derivative (octabromodiphenyl ether, OctaBDE)

Synonyms: octabromobiphenyl oxide; octabromodiphenyl oxide; octabromo phenoxybenzene and benzene; 1,1' oxybis-, octabromo derivative
CAS Number: 32536-52-0
Molecular formula: $C_{12}H_2Br_8O$
Molecular weight: 801.38

Chemical structure: (x+y=8)



Three polybrominated diphenyl ether flame retardants were historically available commercially. They are referred to as penta, octa and decabromodiphenyl ether, but each product is a mixture of diphenyl ethers with varying degrees of bromination. Several synonyms and abbreviations for polybrominated diphenyl ethers exist and these are shown below:

polybrominated biphenyl ethers ≡ polybromobiphenyl ethers – PBBEs
polybrominated biphenyl oxides = polybromobiphenyl oxides - PBBOs
polybrominated diphenyl ethers ≡ polybromodiphenyl ethers - PBDPEs
polybrominated diphenyl oxides = polybromodiphenyl oxides – PBDPOs

The abbreviations PBDE and BDE preceded by the number of bromine atoms (e.g. HeptaBDE) will be used in this document. The commercial mixtures will be identified by a c- (e.g. c-OctaBDE).

The compositions of the commercial polybrominated diphenyl ethers based on composite samples from the EU suppliers are shown in Table 1-1below. These are the substances that have been used in the recent tests and used as a basis for the EU risk assessment reports (RAR) for the three commercial substances. La Guardia et al (2006) have recently reported additional information on the composition of commercial mixtures.

The commercial mixture covered by this entry is therefore a complex combination of isomers and congeners, as defined at POPRC. This risk profile will focus on the series of Hexa, Hepta, Octa and Nona homologues, as the Penta and Deca homologues are covered by their respective commercial mixtures. There is a tendency in scientific literature to present the identities of polybrominated diphenyl ether congeners using the numbering system based on the polychlorinated biphenyl system:

- Hexabromodiphenyl ethers (benzene, 1,1'-oxybis-, hexabromo derivative; HexaBDE) (CAS No. 36483-60-0; IUPAC N° between BDE-128 and BDE-169)
- Heptabromodiphenyl ethers (benzene, 1,1'-oxybis-, heptabromo derivative; HeptaBDE) (CAS No. 68928-80-3; IUPAC N° between BDE-170 and BDE-193)
- octabromodiphenyl ethers (benzene, 1,1'-oxybis-, octabromo derivative; OctaBDE) (CAS No. 32536-52-0; IUPAC N° between BDE-194 and BDE-205)
- Nonabromodiphenyl ethers (benzene, 1,1'-oxybis-, nonabromo derivative; NonaBDE) (CAS No. 63936-56-1; IUPAC N° between BDE-206 and BDE-208)

Table 1-1. Composition of commercial polybrominated diphenyl ethers as described in the EU RAR.

Component	% Composition of commercial product			
	Penta-		Octa-	Deca-
	1997	2000	1997	1997
Tribromodiphenyl ether		0.23		
Tetrabromodiphenyl ether	33.7	36.02		
Pentabromodiphenyl ether	54.6	55.10		
Hexabromodiphenyl ether	11.7	8.58	5.5	
Heptabromodiphenyl ether			42.3	
Octabromodiphenyl ether			36.1	0.04
Nonabromodiphenyl ether			13.9	2.5
Decabromodiphenyl ether			2.1	97.4

The complexity for setting a risk profile for a complex mixture has been already discussed by the POPRC with reference to the commercial mixture of pentabromodiphenyl ether. A full data set for conducting a risk profile is not available for the commercial mixture or for the individual components. Thus the available pieces of information have been combined in this risk profile. The information was particularly scarce for Hepta- to NonaBDEs but there is an increasing interest in the scientific community for covering these congeners. A quantitative assessment is still not possible nowadays, but may become feasible soon if additional scientifically sound information is produced at a similar rate than in recent years,

1.2 Conclusion of the POP Review Committee of Annex D informat*ion*

The POPRC has evaluated Annex D information and has concluded that proposal fulfils the requirements of Article 8 and Annex D of the Convention (POPRC-2/6)

1.3 Data sources

The EU risk assessment report (EC, 2003), the Canadian assessment (Environment Canada, 2004), and references from the WHO (1994) report were the main source of information used by the POP RC in Annex D screening. Additional information has been submitted by Canada, the Czech Republic, Germany, Japan, Lithuania, Norway, Switzerland, Turkey, UK, USA, the NGO Environmental Health Fund on behalf of the International POPs Elimination Network (IPEN), and the industry organization Bromine Science and Environmental Forum (BSEF), as well as during the consultation period. Considering the large amount of new scientific information produced nowadays, a review of recent scientific literature has also been conducted and used as an essential data source in this report.

1.4 Status of the chemical under international conventions

- OSPAR Convention: OctaBDE is included in the list of selected substances for the OSPAR lists (no 236). Under the reviewed list, OctaBDE is put under section C – about the substances put on hold because they are not produced and/or used in the OSPAR catchment or are used in sufficiently contained systems making a threat to the marine environment unlikely.
- UNECE, Convention on Long-range Transboundary Air Pollution (LRTAP) and its Protocol on Persistent Organic Pollutants (POPs): c-OctaBDE is being considered under Protocol procedures for inclusion.

2. Summary information relevant for the risk profile

2.1 Sources

The information provided by the bromide industry indicates that the commercial product has been produced in The Netherlands, France, USA, Japan, UK and Israel, but since 2004, it is no longer produced in the EU, USA and the Pacific Rim and there is no information that indicates it is being produced in developing countries.

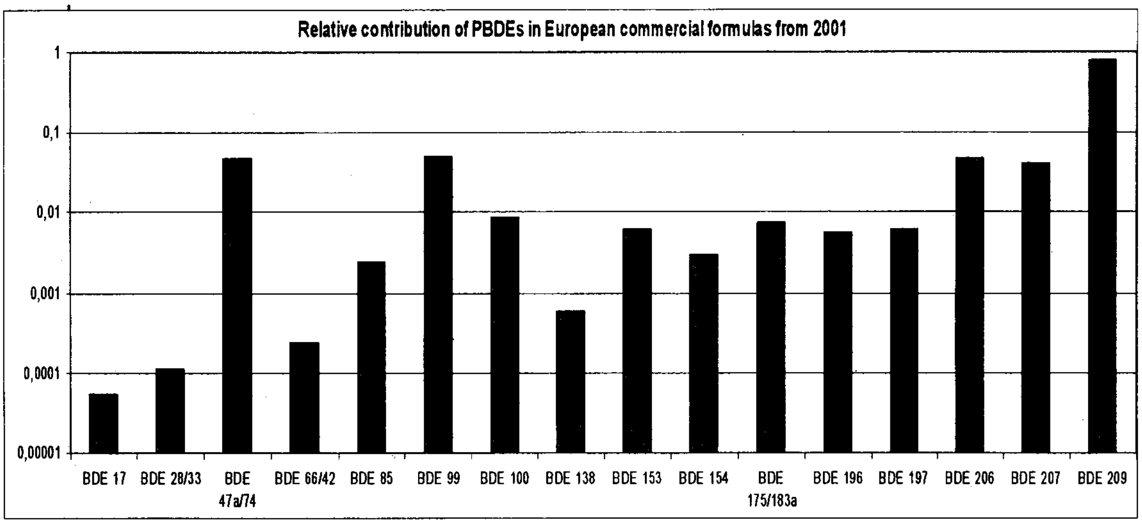
The polybrominated diphenyl ethers in general are used as flame retardants of the additive type. They are physically combined with the material being treated rather than chemically combined (as in reactive flame retardants). This means that there is the possibility that the flame retardant may diffuse out of the treated material to some extent. Industry indicates that octabromodiphenyl ether is always used in conjunction with antimony trioxide. In Europe, it is primarily used in acrylonitrile-butadiene-styrene (ABS) polymers at 12-18% weight loadings in the final product. Around 95% of the total octabromodiphenyl ether supplied in the EU is used in ABS. Other minor uses, accounting for the remaining 5% use, include high impact polystyrene (HIPS), polybutylene terephthalate (PBT) and polyamide polymers, at typical loadings of 12-15% weight in the final product. In some applications, the flame retardant is compounded with the polymer to produce pellets (masterbatch) with slightly higher loadings of flame retardant. These are then used in the polymer processing step to produce products with similar loadings as given above.

The flame retarded polymer products are typically used for the housings of office equipment and business machines. Other uses that have been reported for octabromodiphenyl ether include nylon and low density polyethylene (WHO, 1994), polycarbonate, phenol-formaldehyde resins and unsaturated polyesters (OECD, 1994) and in adhesives and coatings (WHO, 1994).

Assuming that the commercial OctaBDE is not longer produced, the releases to the environment must be associated to historical processes, as well as to releases during the service life of articles containing the commercial mixtures and at the end of article service life during disposal operations. The information review by La Guardia et al (2006) allows estimations of the relative contribution of each congener in different markets and time periods. As an example, Figure 1-1 presents the calculations for European commercial products in 2001.

Although there are some figures on annual production of this mixture, there are no accurate values on the amount of the commercial Octa and/or the individual homologues in articles in service and disposed at the world-wide level, but considering the estimated figure of 6 000 tonnes/year (WHO, 1994) the total amount should be expected in the $10^5 - 10^6$ tonnes range. According to the BSEF, OctaBDE was commercialized sometime in the mid 70's. By the early 2000's global production was <4000 tonnes/year and by the time production ceased, demand was <500 tonnes. While thus, assuming 30 years of production at 6000 tonnes per year gives 180,000 tonnes, a figure within the proposed range.

Figure 1-1. Estimated relative contribution for the different BDE congeners in products in the European market in 2001. Calculated from data published by La Guardia et al., 2006. Note the logarithmic scale.



Morf et al., (2002) reported for Switzerland diffuse emission from the use of products containing OctaBDE of about 0.37 t/a (based on worst-case estimations) for a total stock of 680 tons.

2.2 Environmental fate

2.2.1 Persistence

No aerobic biodegradation of the Hexa- to NonaBDEs is expected based on BIOWIN estimates as recalcitrant with respect to biodegradation, and no degradation, based on oxygen uptake, occurred in a 28-day closed bottle test OECD 301D (EC, 2003).

Gerecke et al. (2005) reported the degradation of NonaBDE 206 and 207 and DecaBDE to OctaBDEs under anaerobic conditions using sewage sludge innoculum; and this degradation has been confirmed in other studies (Gaul et al, 2006; He et al, 2006).

AOPWIN predicts half-lives for reaction with atmospheric hydroxyl radicals ranging from 30.4 to 161.0 d for Hexa- to NonaBDEs, respectively. However, in the atmosphere, Hexa to NonaBDEs are expected to strongly adsorb to suspended particles in the air and be removed via wet and/or dry deposition. Note that predicted half-lives have not been empirically substantiated, but are provided for reference purposes.

The photodecomposition of several BDEs has been studied in different matrices such as sealed polyethylene tube exposed to natural sunlight for up to 120 min (Peterman et al. 2003); or water (Sanchez-Prado et al., 2006); in general degradation was faster for the higher brominated DEs than for the lower brominated congeners. Rayne et al. (2006) suggest a short photochemical half-life for the Hexa BDE153 in aquatic systems, with rapid photohydrodebromination to some of the most prevalent Penta- and Tetra-brominated diphenyl ether congeners.

2.2.2 Bioaccumulation

The bioaccumulation potential differs strongly among the components of the commercial mixture. For facilitating, the assessment, the different bioaccumulation processes will be presented independently.

2.2.2.1. Bioconcentration from water

Bioconcentration from water is considered relevant only for HexaBDE. The UK has re-analyzed the CITI (1982) bioconcentration data and suggests BCFs of up to ~5,640 l/kg and ~ 2,580 l/kg for components D and E (both HexaBDE).

Bioconcentration factors were reported (EC, 2003) for carp. Assuming that the actual concentrations of the c-OctaBDE components were at or around the reported water solubility for the substance of 0.5 µg/L, then the BCF for OctaBDE would be <9.5; for HeptaBDE about <1.1-3.8 and for c-OctaBDE about <10-36. These BCF values are lower than would be expected from the substance's octanol-water partition coefficients. This can be explained by a reduced bioavailability, metabolisms or both.

2.2.2.2 Bioaccumulation and biomagnification from food exposures.

Oral exposure is expected to be the most relevant exposure pathway for these chemicals. Van Beusekom et al. (2006) reported biota-sediment accumulation factors between 1 and 3 for Hexa and HeptaBDE on two freshwater fish species in Spain and concluded that 100% of the exposure was associated to food or food plus sediment for bleak (Alburnus alburnus) and barbel (Barbus graellsii), respectively.

A controlled feeding trial assessed transfer and accumulation of PBDEs from feed to farmed Atlantic salmon (Salmo salar). On average, 95% of the total PBDE content in the feed accumulated in whole salmon including HeptaBDE 183 (Isosaari, et al. 2005).

The potential for biomagnification has been demonstrated for Hexa and HeptaBDE (Burreau et al., 2004; 2006; Sormo et al., 2006; Tomy et al., 2004), and more recently suggested for the DecaBDE (Law et al., 2006).

Food-web biomagnification was not been observed for Octa and NonaBDE in an aquatic ecosystem, but the congeners were detected in biota from zooplanckton to fish species (Burreau et al. 2006).

2.2.2.3. Bioaccumulation from sediment exposures

Ciparis and Hale (2005) have reported a rapid bioaccumulation of HexaBDE in the aquatic oligochaete, *Lumbriculus variegates*, exposed via sediment, with differences between isomers and in the contamination pathway. A biota-sediment accumulation factor of 9.1± 1.1 was observed for BDE 154, the highest concentration was found on day 15 and the depuration rate constant was 0.032 ± 0.016 days^{-1}.

2.2.2.4. Toxicokinetics and relevance of metabolisms

The potential for bioaccumulation and biomagnification of these types of molecules can be calculated using toxicokinetic models, based on metabolism and elimination. Differences among isomers and the reported debromination processes introduce additional uncertainty when reviewing field data.

Stapleton et al. (2004) in a dietary study on carps found depuration rates of 0.051± 0.036 days^{-1} and assimilation efficiencies of 4% ± 3 for the HexaBDE 153. Stapleton and Baker (2003) and Stapleton et al. (2004b) in dietary studies on common carp (*Cyprinus carpio*) found significant and rapid debromination of HeptaBDE183 to HexaBDE154 and to another unidentified HexaBDE congener within the intestinal tissues of the carp after consuming its food. *In vitro* studies have demonstrated the microsomal debromination in fish (Stapleton et al. (2006).

Tomy et al (2004) exposed juvenile lake trout (*Salvelinus namaycush*) to three dietary concentrations of 13 BDE congeners (3-10 Br atoms) in the laboratory for 56 days, followed by 112 days of clean food. Half-lives (t1/2's) for some BDE congeners (e.g., BDE-85 and -190) were much lower than expected based on their Kow, whereas t1/2's of other BDE congeners (e.g., BDE-66, -77, -153, and -154) were much longer than anticipated based on Kow. This was explained by debromination. The detection of three BDE congeners (an unknown PentaBDE, BDE-140, and an unknown HexaBDE) in the fish that were not present in the food or in the control fish provided further evidence for the debromination of BDEs.

The role of exposure levels in the elimination rate of several chemicals including HexaBDE 153 has been studied by the LPTC). Université Bordeaux I and the INIA's Laboratory for Ecotoxicology within the context of LRI-Cefic Research Project ECO-1AINIA-1100. Depuration rates of 0.03-0.05 for *Sparus aurata* and *Mytilus edulis*, were obtained (Alonso et al., 2006).

The debromination of PBDEs has also indicated in mammals, e.g. for a c-PentaBDE formulation in mice (Qiu et al., 2007) and for DecaBDE in cows (Kierkegaard et al., 2007).

A recent study (Drouillard et al., 2007) has reported a depuration rate constant for the HexaBDE 0.016 days^{-1} in juvenile American kestrels (*Falco sparverius*), with a retention of about 50% of the administered dose in a 36 days study.

Van den Steen et al. (2007) used silastic implants to expose European starlings (Sturnus vulgaris) to DecaBDE209 and found Octa- (BDE196, BDE197) and NonaBDEs (BDE206, BDE207, BDE208) in muscle and liver in addition to DecaBDE209, resulting in the first indications of debromination in birds.

2.2.2.5 *Integrated assessment of the bioaccumulation potential.*

A high potential for bioaccumulation (including a moderate potential for bioconcentration) and food-web biomagnification has been demonstrated for HexaBDE; and it is fully in line with the reported elimination rates.

The food-web biomagnification has been also demonstrated for HeptaBDE, although at a lower extend than expected from the Kow; this fact can be explained by metabolism resulting in a relatively short half-life (experimentally demonstrated and explained by the authors by debromination).

The presence of Octa and NonaBDE in biota is well document but its potential for bioaccumulation from water and food is much lower than expected from their Kow. Reduced availability, metabolisms or both can justify this fact. The number of scientific papers demonstrating debromination of Deca-, Nona, and Octa- BDE to other PBDEs is continuously increasing; this is critical for the assessment as would indicate that the supposed low bioaccumulation potential could be in reality the consequence of metabolism to bioaccumulative PBDEs. A quantitative estimation cannot be presented yet, but the debromination process has been already reported for aquatic organisms, mammals and birds.

2.2.3 Long range environmental transport

The presence of components of commercial Octa BDE in remote areas (e.g. Norway info, Norway Info 2; Canada info 2; Switzerland info2, Japan info) is considered the best demonstration for the potential for long range transport of these chemicals. As debromination in biota has been demonstrated, hypothetically, the presence of Hexa to NonaBDEs could be explained by a long range transport of DecaBDE and its subsequent debromination, however, since Hexa to Deca congeners have similar atmospheric transport characteristics in terms of gas-partitioning and reactivity it is evidence of long range transport for DecaBDE and is indirect evidence of long range transport for the Nona to Hexa congeners.

Previous model predictions suggested a low potential for long-range atmospheric transport for highly brominated BDEs (e.g. Wania and Dugani, 2003). However, in a recent paper on DecaBDE, Breivik et al., (2006) have reported that chemicals that are both sorbed to particles and potentially persistent in the atmosphere, such as BDE-209, may have a larger potential for LRT than anticipated on the basis of earlier model evaluations. This explanation could be also applied to c-OctaBDE components.

Recently Wegmann, et al, (2007) applied the OECD Pov and LRTP Screening Tool to the current POPs candidates, including c-OctaBDE. The authors noted that they believed that the substance property values for c-OctaBDE in Wania and Dugani (2003) were more accurate than the values in the POPRC document and therefore included the Wania and Dugani values in their Monte Carlo uncertainty analysis. Although there were considerable uncertainties, the results indicated that c-OctaBDE has Pov and LRTP properties similar to those of several known POPs.

2.3 Exposure

2.3.1 Atmosphere

Strandberg et al. (2001) analyzed air samples from urban, rural and remote sites in the United States near the Great Lakes. The average total c-OctaBDE-related congeners (i.e., sum of BDEs 153, 154 and 190) present in the samples ranged from approximately 0.2 to 0.9 pg/m3.

Bergander et al. (1995) analyzed air samples from two areas of Sweden remote from industry, HexaBDE and HeptaBDE were found in the particulate phase samples.

In a monitoring study carried out in coastal areas of Korea over one-year period, twenty individual PBDE congeners were found in atmospheric samples collected from urban, suburban and rural sites. DecaBDE (BDE 209) was the predominant congener (<93%) The depositional fluxes ranged from 10.1 to 89.0 µg/m2/year (Moon et al., 2007a). In northwest China, the measurements of total PBDEs (8.3 ± 4.0 pg/m3) in the samples collected at the Waliguan Baseline Observatory (April to May, 2005) were at comparable concentration levels with other remote areas (Cheng et al., 2007).

PBDEs have also been detected over the Indian Ocean (mean concentration of 2.5 pg/m3) and along the coastal line of Java, Indonesia (values of 15 pg/m3). Air back trajectory analysis is suggested in relation to the potential of PBDEs for long-range atmospheric transport from remote regions of areas more industrialized (Wurl et al. 2006).

Wang et al. (2005,) report atmospheric concentrations for c-OctaBDE components for a large number of remote locations, and additional information about the presence of Penta to HeptaBDE congeners in air at several locations can be found in the review paper by de Wit et al. (2006).

2.3.2 Water

Luckey et al. (2002) measured total PBDE (mono- to HeptaBDE congeners) concentrations of approximately 6 pg/L in Lake Ontario surface waters in 1999, with HexaBDE congeners BDE153 and BDE154 each contributing approximately 5 to 8% of the total.

C-OctaBDE was not detected in 1987 in 75 surface water samples taken in Japan at a detection limit of 0.1µg/L or in 1988 in 147 water samples at a detection limit of 0.07 µg/L (Environment Agency Japan 1991). According to EC (2003), the concentrations are considered to be representative of industrial, urban and rural areas of Japan, but it is not known whether any of the sampling sites were in the vicinity of a polybrominated diphenyl ether production site or a polymer processing site.

There is additional information on concentrations of c-OctaBDE components (HexaBDEs 153 and 154) in the dissolved phase in water in a study by Law et al. (2006).

2.3.3 Sediments

Concentrations of c-OctaBDE in UK sediments ranged from <0.44 to 3030 µg/kg dw (Allchin et al. 1999; Law et al. 1996; Environment Agency UK, 1997)). The highest levels were in sediments downstream from a warehouse where c-DecaBDE was stored. C-OctaBDE was detected in 3 of 51 sediment samples from Japan in 1987 at concentrations from 8 to 21 µg/kg (detection limit 7 µg/kg; ww or dw not specified), and in 3 of 135 samples collected in 1988 at concentrations of 15 to 22 µg/kg (detection limit 5 µg/kg; ww or dw not specified) (Environment Agency Japan 1991).

Kolic et al. (2004) presented levels of PBDEs in sediments from tributaries flowing to Lake Ontario, and area biosolids in southern Ontario. Total Hexa- and HeptaBDEs (i.e., BDE 138, 153, 154 and 183) measured in sediment samples taken from fourteen tributary sites (only 6 sites were reported) ranged from approximately 0.5 to 4.0 µg/kg dw.

Historical trends of PBDEs in sediments have been determined in the Lake of Ellasjøen, Norwegian Arctic, where contamination is due to both atmospheric and biological transport. Maximum level of PBDEs was detected in 2001 (0.73 ng/g dw) (Evenset et al., 2007). Marvin et al. 2007, have reported temporal trends in PBDEs in Niagara river suspended sediments from 1988 to 2004. Prior to 1988, PBDEs (sum of 16 congeners including DecaBDE) were generally detected at low-ppb concentrations, but showed a trend toward increasing concentrations over the period 1980–1988. After 1988, PBDE concentrations in the Niagara River showed a more rapidly increasing trend (maximum of approximately 35 ng/g in 1995). DecaBDE was the predominant congener detected, and a similar situation has been observed in Europe (Eljarrat et al., 2005), and Asia (Moon et al. 2007b).

The study by Law et al. (2006) provides additional information on concentrations of c-OctaBDE components (HexaBDEs 153 and 154) for sediments at a background location.

2.3.4 Soil

Hassanin et al. (2004) determined PBDEs in undisturbed surface soils (0-5 cm) and subsurface soils from remote/rural woodland and grassland sites on a latitudinal transect through the United Kingdom and Norway. In total, 66 surface soils were analyzed for 22 tri- to HeptaBDEs. Concentrations of total PBDEs in the surface soils ranged from 0.065 to 12.0 µg/kg dw. Median PBDE concentrations in the surface soils ranged from 0.61 to 2.5 µg/kg dw, with BDEs 47, 99, 100, 153 and 154 dominating the total concentrations. The median concentration of the sum of these five congeners ranged from 0.44 to 1.8 µg/kg dw. The researchers noted that the congener patterns in the European background soils closely matched that reported for the c-PentaBDE mixture. Northward along the latitudinal transect, there was an increasing relative contribution of BDE 47 and other lighter PBDEs in comparison to the heavier PBDEs measured in the samples.

2.3.5 Waste Effluent and Biosolids

Kolic et al. (2004) presented levels of PBDEs in sediments from tributaries flowing to Lake Ontario, and of biosolids from nearby wastewater treatment facilities in southern Ontario. Total Hexa- and HeptaBDEs (i.e., BDEs 138, 153, 154 and 183) measured in biosolids ranged from approximately 111 to 178 µg/kg dw.

La Guardia (2001) analyzed 11 sewage sludge samples before land application from Canada and the United States and found that total Hexa- to OctaBDE congener concentrations ranged from 40 to 2080 µg/kg dw. Kolic et al. (2003) investigated PBDE levels in sewage sludge from 12 sites in southern Ontario and found Hexa- to OctaBDE congener concentrations totaled 124 to 705 µg/kg dw. Hexa- to OctaBDE congeners were not detected in manure samples, and were at very low levels in pulp mill biosolids (up to approximately 3 µg/kg dw).

Martinez et al. (2006) have recently reported concentrations of sum of Hexa to NonaBDE in the range of 15.5 to 160 µg/kg dw in sludge from municipal wastewater treatment facilities in Spain, and up to 268 µg/kg dw in industrial facilities.

Gevao et al. (2006) measured PBDEs in coastal sediments receiving industrial and municipal effluents in Kuwait. Total concentrations varied from 80 to 3800 pg/g dw with HeptaBDE183 dominating the congener distribution which resembled the commercial formulation, Bromkal 79-8DE. Wastewater discharge from industrial activities appeared to be the primary source of the compounds.

2.3.6 Biota

Concentrations of components found in c-OctaBDEs in biota were reviewed in Law et al. (2003). The concentration of c-OctaBDE (reported as the commercial mixture DE-79) in various biota found in aquatic environments in the UK ranged up to 325 µg/kg ww in the liver of dab (Allchin et al. 1999). Concentrations of OctaBDE in muscle tissue from UK fish ranged from <1 to 12 µg/kg ww (Allchin et al. 1999). In Japan, OctaBDE was not detected in 75 fish samples taken in 1987 (detection limit 5 µg/kg ww), nor was it detected in 144 fish samples taken from 48 locations in 1988-89 (detection limit 4 µg/kg; ww or dw not specified) (Environment Agency Japan 1991). HeptaBDE, along with other PBDE congeners, was detected in eggs of peregrine falcons, *Falco peregrinus*, from Sweden, at concentrations from 56 to 1300 µg/kg lipid (Lindberg et al. 2004).

Alaee et al. (1999) sampled lake trout from Lakes Superior, Huron and Ontario and found that the total of HexaBDE and HeptaBDE congeners ranged from an estimated 11 to 53 µg/kg lipid.

Rice et al. (2002) compared PBDE levels and congener patterns in carp and bass sampled from two industrialized regions in the eastern U.S. The fish were collected from the Detroit River, MI. and the Des Plaines River, IL. in May and June of 1999, and analyzed for the presence of BDEs 47, 99, 100, 153, 154, 181, 183 and 190. Both river systems are considered to receive high contributions from municipal and industrial effluents. BDE47 dominated in fish taken from the Detroit River, comprising an average of 53 to 56% of the total PBDEs by wet weight. BDEs 99, 100, 153 and 154 each contributed between 8 and 9%, and BDEs 181 and 183 each comprised about 5% of the total PBDEs. BDE190 was not detected in either fish species. Only carp were sampled from the Des Plaines River, and these exhibited a markedly different PBDE profile from that seen in the Detroit River fish. HeptaBDEs 181 and 183 were predominant, contributing about 21% and 19%, respectively. BDE47 was third in prevalence, comprising about 17% of the total PBDEs. Levels of the two HexaBDE congeners, BDEs 153 and 154 were 8 to 13%, compared with about 5% for each of the Penta- congeners, BDEs 99 and 100. BDE190, not detected in the Detroit River fish, was present at about 12% of total PBDE.

Norstrom et al. (2002) evaluated the geographical distribution and temporal trends (during the 1981 to 2000 period) of PBDEs in herring gull (*Larus argentatus*) eggs from a network of colonies scattered throughout the Great Lakes and their connecting channels in 2000 (see Section 2.1.6.6 and Appendix D). Although samples were analyzed for Octa- to DecaBDE, these were not found at their respective limits of detection (0.01-0.05 µg/kg ww). However, total concentrations of Hexa- and HeptaBDE congeners (i.e., BDEs 153,154 and 183) increased 6 to 30 fold over the 1981 to 2000 period at the Lake Michigan (from 6.7 to 195.6 µg/kg ww), Lake Huron (from 13.8 to 87.6 µg/kg ww) and Lake Ontario (3.8 to 112.1 µg/kg ww) sites. This increase was not as dramatic as that found for the tetra- and PentaBDE congeners.

Wakeford et al. (2002) conducted sampling of wild bird eggs in western and northern Canada between 1983 and 2000. They determined that the total of Hexa- and HeptaBDE congeners ranged from 0.148 to 52.9 µg/kg ww in Great Blue Heron (*Ardea herodias*) eggs (on Canada's west coast), 0.03 to 0.68 µg/kg ww in Northern Fulmer (*Fulmarus glacialis*) eggs (in the Canadian arctic) and 0.009 to 0.499 µg/kg ww in Thick Billed Murre (*Uria lomvia*) eggs (in the Canadian arctic). OctaBDE, NonaBDE and DecaBDE congeners were subject to analysis by the researchers, but were not detected (detection limit was not specified) in the any of the samples.

Temporal, spatial, and interspecific trends in PBDEs were determined in eggs of marine and freshwater bird species from the province of British Columbia, Canada. Temporal trends in the Fraser River estuary, 1983-2002, were examined by analysis of eggs of great blue herons (Ardea herodias) and from the Strait of Georgia marine ecosystem, 1979-2002, in eggs of double-crested cormorants (Phalacrocorax auritus). PBDEs increased exponentially with a doubling time of 5.7 years in eggs of both herons and cormorants. The PBDE pattern was relatively consistent in most years and sites, with BDEs 47 > 100 > 99 > 153 > 154 > 28 > 183. This was interpreted as evidence of technical PentaBDE formulations as primary sources of the contamination, with the OctaBDE formulations as secondary. Higher resolution analysis of a subsample of the eggs revealed the presence of up to nine other congeners, including BDE209 (range: 0.9-1.8 microg/kg), indicating exposure and uptake of DecaBDE sourced congeners in North American foodchains (Elliot et al., 2005)

A recent study (Burreau et al., 2006) has demonstrated the presence of Hexa to NonaBDE in biota (zooplankton, sprat, herring and salmon) from the Baltic Sea and Northern Atlantic.

2.3.7 Humans

EC (2003) presents some information on the levels of components of c-OctaBDE measured in human samples including human milk, blood, and adipose tissue. Large variations among individuals were generally observed, but significant differences between the control population and occupationally exposed groups were also reported.

In a recent study (Toms et al., 2007) the concentrations of PBDEs (18 congeners from BDE17 to BDE-183) found in Australian human milk were lower than those reported from North America but higher than those reported from Europe and Asia

Thomsen et al., 2007, investigated the levels of PBDEs in 21 pooled serum samples archived from the general Norwegian population (from 1977 to 2003). In serum from men (age 40–50 years) the sum of seven PBDE congeners (28, 47, 99, 100, 153, 154 and 183) increased from 1977 (0.5 ng/g lipids) to 1998 (4.8 ng/g lipids). From 1999 to 2003 the concentration of PBDEs seems to have stabilised.

Fernandez et al., 2007, have reported a study of the detection of PBDEs in the adipose tissue of women from Spain. Mean ∑PBDE (BDE 28, 75, 71, 47, 66, 77, 100, 119, 99, 85, 154, 153, 138, and 183) levels were 3.85 and 0.36 ng/g of lipid, respectively. Among PBDEs, congeners 153, 47, 183, 99, and 100 were the most frequent and abundant and together constituted 96% of the total amount of PBDEs in adipose tissue. Concentrations of PBDEs in this population were similar to those reported in other parts of Spain and in Swedish and Belgium populations but lower than those found in other Western countries.

PBDEs were measured in samples of human blood serum taken from 23 donors in Wellington, New Zealand. Concentrations expressed as the sum of congeners 47, 99, 100, 153, 154, and 183 (∑PBDE) were – at an average of 7.17 ng ∑PBDE g $(\text{lipid})^{-1}$ – within the range reported for human tissues in Europe, but lower than in Australia and North America (Harrad et al., 2007).

Based on the measured PBDE levels detected in various meat, fish and dairy food products, an average daily dietary intake estimate of PBDEs was calculated in a study carried out in Belgium. PBDE intake calculations were estimated between 23 and 48 ng/day of total PBDEs. Fish is the major contributor to the total daily PBDE-intake (around 40%) due to the high PBDE levels in this type of food, although it is only a minor constituent of the Belgian diet. Meat products account for around 30% of the total dietary intake of PBDEs. Dairy products and eggs contribute to a lesser degree (less than 30%, Voorspoels et al., 2007).

Schuhmacher et al., 2007 have carried out an study to compare levels of PBDEs due to dietary intake and population living near a hazardous waste incinerator (HWI), in Spain. This study suggests that dietary intake is more relevant for human exposure to PBDEs than living near the HWI. Dietary intake of PBDEs for standard adult women were 72 and 63 ng/day for PBDEs, for residents in urban and industrials areas, respectively. Mean PBDE concentrations were 2.2 and 2.5 ng/g fat for women living in urban and industrial zones, respectively. Similar results have also been reported in a study carried out in Korea (Lee et al., 2007)

Exposure to components of c-OctaBDE in remote areas is confirmed and based on the available information should be attributed to a combination of releases and transport of c-OctaBDE, c-PentaBDE (for HexaBDE) and c-DecaBDE (for NonaBDE), and to the debromination of DecaBDE in the environment including biota. There is no sufficient information for assessing these processes in quantified terms. The exposure route is mainly via food. In addition to the feeding strategy, several additional confounding factors are associated to the species to specific differences observed in the isomer distribution pattern of PBDE in wildlife. These factors include, among others, species-specific differences in assimilation, metabolism and depuration of different isomers, even with the same level of bromination.

Measured levels of Hexa and Hepta components of c-OctaBDE in biota from remote areas seem to be the best available information for estimating exposure as result of LRET for these chemicals. Knudsen et al (2005) have recently review temporal trends of PBDE in eggs from three bird species, three locations and three sampling times (from 1983 to 2003) from Northern Norway. Spatial differences were only observed for HexaBDE 153, and increases in the measured concentration from 1983 to 2003 were observed for the HexaBDE 153 and 154 and the HeptaBDE 183. Mean values were around 1 µg/kg ww for each isomer and maximum values above 10 µg/kg ww were observed for BDE 154 and 183. Inter-species differences could be associated to feeding behavior and migration. In general the concentrations were lower than those reported for similar species in industrialized areas and those observed in terrestrial predatory birds. The presence of Hexa and HeptaBDE in fish from remote alpine lakes in Switzerland (Schmid et al., 2007) reported to be related to atmospheric deposition confirms the potential for atmospheric long-range transport. Hexa to NonaBDE have been found in salmon in the Atlantic Ocean west of Iceland (Burreau et al. 2006).

Despite its large molecular size, the evidence demonstrates the capability of c-OctaBDE components to cross the cellular membranes and to accumulate in biota. Although the information is limited, the assimilation and metabolisms of each isomer may vary significantly among species, but also in relation to the administered dose. As a consequence, it is essential to understand the toxicokinetics of these chemicals at environmentally relevant concentrations. These differences would justify the disparities observed in the assessment of biomagnification potential for different trophic chains.

Like for other chemicals with similar properties, aging processes are expected to reduce the bioavailability, and the experiments conducted on sediment dwelling organisms comparing the bioaccumulation in spiked sediments and from contaminated biosolids offer and indirect support for this hypothesis.

2.4 Hazard assessment for endpoints of concern

2.4.1. Experimental studies

2.4.1.1. Aquatic Organisms

The EU Risk Assessment report (EC, 2003), presents a set of studies on the commercial mixture and concludes that for water it seems sensible to assume that no adverse effects on aquatic organisms are likely to occur at concentrations up to the substance's water solubility. However it must be noted, first, that aquatic organisms are also exposed from food and/or sediment; and second, that setting this strong conclusion on chemicals such as PBDEs requires multigenerational or at least full life-cycle assays on the three taxonomic groups covering a large list of sublethal effects, information which is unavailable at this time.

2.4.1.2. Benthic Organisms

There are two available 28 day spiked sediment studies on *Lumbriculus variegatus* using the c-OctaBDE product (Great Lakes Chemical Corporation 2001a, b). These studies found no statistically significant effects relevant to survival, reproduction or growth at the highest tested concentration (1272 mg/kg dw and 1340 mg/kg dw measured for sediments with 2.4% and 5.9% OC, respectively). Kinetic data from Ciparis and Hale (2005) confirms the expected exposure and bioaccumulation under these conditions.

2.4.1.3. Soil Organisms

Survival and growth of earthworms, *Eisenia fetida,* were not affected by a 56 day exposure to a commercial OctaBDE formulation in an artificial soil at concentrations up to 1470 mg/kg dw (measured concentration in sediments with 4.7% OC) (Great Lakes Chemical Corporation 2001c).

The toxicity of c-OctaBDE to corn (*Zea mays*), onion (*Allium cepa*), ryegrass (*Lolium perenne*), cucumber (*Cucumis sativa*), soybean (*Glycine max*), and tomato (*Lycopersicon esculentum*) was evaluated in a 21-day emergence and growth study using an artificial sandy loam soil (Great Lakes Chemical Corporation 2001d). No statistically significant effects were observed for any plant species between the controls and the treatments for emergence, survival or growth at any of the tested concentrations (up to 1190 mg/kg dw, measured concentration).

2.4.1.4. Mammals and Birds

The lowest reported NOAEL for traditional endpoints is a NOAEL of 2 mg/kg/d based on slight fetotoxicity at 5 mg/kg/d (considered relevant in the EU report) or 5 mg/kg bw/d based on increased liver weights and decreased body weight gain among the maternal treatment group and delayed fetal skeletal ossification at 15 mg/kg bw/d (for those reviewers that do not consider relevant the slight fetotoxicity effects) described by Breslin et al. (1989) in a developmental toxicity study with Saytex 111 on New Zealand White rabbits exposed orally via gavage over days 7 to 19 of gestation.

Effects on other endpoints have been described at lower concentrations, including:

- A significant increase in EPN detoxification and *p*-nitroanEROD and isole demethylation in male Sprague-Dawley rats at an oral dose of 0.60 mg/kg bw/day OBDE formulation for 14-days.
- dose-dependent depletion of serum total thyroxine T4 and induced pentoxyresorufin *O*-deethylase (PROD) activities in rats receiving 10 or more mg/kg bw/day of commercial OctaBDE (Zhou et al. 2001)
- Delayed neurotoxic effects. Neonatal mice exposed to a single dose of 0.45 mg BDE153/kg bw on postnatal day 10 showed when tested at 2, 4 and 6 months of age altered motor behavior. Spatial learning ability and memory function in the adult mice were also affected (Viberg et al.,2001)
- Eriksson et al. (2002) confirmed neurotoxic effects (aberrant behavioral responses) on developing male mice exposed to 0.45 to 9.0 mg/kg bw of BDE153 on day 10 of development. The effects were comparable to those

observed for PCB153 leading the authors to speculate that interactive neurotoxic action may be possible between the two compounds.

- These neurotoxic effects have also been observed after a single oral dose of NonaBDE 206 or OctaBDE 203 administered on postnatal day 3 or 10 to, or PBDE 183; with disturbances in spontaneous behavior, leading to disrupted habituation and a hyperactive condition in adults at the age of 2 months. (Viberg et al., 2006).
- Immunomodulation effects in captive nestling American kestrels (*Falco sparverius*) have been reported by Fernie et al. (2005). Eggs within each clutch, divided by laying sequence, were injected with safflower oil or PentaBDE congeners-47, -99, -100, and -153 dissolved in safflower oil (18.7 µg PBDEs/egg). For 29 days, nestlings consumed the same PBDE mixture (15.6+/-0.3 ng/g body weight per day), reaching PBDE body burden concentrations that were 120x higher in the treatment birds (86.1+/-29.1 ng/g ww) than controls (0.73+/-0.5 ng/g ww). PBDE-exposed birds had a greater PHA response (T-cell-mediated immunity), which was negatively associated with increasing BDE-47 concentrations, but a reduced antibody-mediated response that was positively associated with increasing BDE-183 concentrations. There were also structural changes in the spleen (fewer germinal centers), bursa (reduced apoptosis) and thymus (increased macrophages), and negative associations between the spleen somatic index and PBDEs, and the bursa somatic index and BDE-47. Immunomodulation from PBDE exposure may be exacerbated in wild birds experiencing greater environmental stresses.
- Fernie et al., 2006 also reported for the same species and test conditions that exposure did not affect hatching or fledging success. PBDE-exposed nestlings were larger (weight, bones, feathers) as they gained weight more quickly and ate more food, the latter in association with their PBDE body burdens. BDE-100 was most influential on nestling growth, being positively associated with size, weight gain, and food consumption. Increasing concentrations of BDE-183 and -153 were related to longer bones and BDE-99 to longer feathers. The larger size of the PBDE-exposed birds may be detrimental to their bone structure and have excessive energetic costs.
- In vitro studies indicates that BDE (including the HexaBDE 153) affected protein kinase C (PKC) and calcium homeostasis in cerebellar granule neuronal cultures in a similar way to those of a structurally-related polychlorinated biphenyl (PCB) (Kodavanti et al., 2005).

Although these studies do not allow a quantitative assessment, they indicate the need for addressing long-term and delayed effects, as well as specific mechanisms of action, in the evaluation of potential health and ecosystem adverse effects.

2.4.2. Monitoring data on effects

There are several scientific papers comparing population effects observed in the field with measured concentrations of POP like chemicals, including Hexa to NonaBDE in individuals from different species.

Unfortunately, wild populations are co-exposed to a mixture of PBDEs as well as to other related brominated and chlorinated persistent pollutants, and with the current level of knowledge epidemiological investigations can just present associations but no cause-effect relationships between the exposure/accumulation of the components of the commercial OctaBDE mixtures and potential adverse effects observed in wildlife.

A similar situation is observed regarding human health data, and no studies offering conclusive evidence on the hazards of Hexa to NonaBDE for humans at environmentally relevant exposure levels have been found.

3. Synthesis of the information

A quantitative evaluation of the specific risks of c-OctaBDE is not possible due to the presence of its components in commercial Penta- and Deca mixtures, and the lack of information; this include the absence of information for supporting quantitative assessments of the role on debromination and the lack of a solid body of toxicological and ecotoxicological information for the mixture and its components; covering the long-term low level exposure conditions and the sublethal endpoints considered relevant for assessing the risk of a POP candidate. Australia and Canada have reported quantitative risk assessments for health and for the environment based on risk quotients and margins of safety suggesting a potential risk. The evaluations do not cover expected conditions in remote areas but are useful in the overall assessment (Environment Canada, 2006; NICNAS, 2007).

In this risk profile, Hexa to NonaBDE have been considered the relevant components in c-OctaBDE. It should be noted that other BDE are also found in commercial mixtures, including those present in c-PentaBDE and c-DecaBDE..

The persistence of these PBDE in the environment is well documented. The only relevant degradation pathways identified until now are photolysis, anaerobic degradation and metabolism in biota, acting through debromination and producing other BDE which may have higher toxicity and bioaccumulation potential.

The bioaccumulation potential depends on the level of bromination. HexaBDE shows a significant potential for bioconcentration and biomagnification; HeptaBDE biomagnifies through the food web but at a lower extend than that expected from the Kow. Octa and NonaBDE have been found in biota but no food-web biomagnification has been observed. Metabolisms and/or reduced bioavailability explain the divergences between observations and Kow predictions. The contribution of metabolism through debromination into other BDEs is supported by and increasingly amount of scientific evidence.

Biota monitoring data in remote areas cover Hexa and HeptaBDE and offer the best demonstration on the potential for long range transport of c-OctaBDE components. Theoretically this presence could also be explained by the transport of DecaBDE and its subsequent debromination. However, it is not realistic to assume that DecaBDE debromination may explain the process without additional transport from other congeners. The role of atmospheric transport is confirmed for Hexa and HeptaBDE based on its detection in alpine lakes.

Unfortunately, the available information on the toxicity and ecotoxicity of Hexa to NonaBDE is very limited and does not offer enough information for presenting sound toxicological and ecotoxicological profiles for each isomer, mixtures of isomers and commercial mixtures.

No relevant effects have been observed in aquatic, sediment and soil laboratory studies; but the measured endpoints and the exposure conditions, employed in these assays are clearly insufficient for a proper assessment of chemicals such as Hexa to NonaBDE. Ecotoxicity tests on these types of chemicals should cover if possible several generations or at least a full life cycle, and the measured endpoints must include sublethal effects associated to the accumulation and re-mobilization of the PBDEs during critical periods of development and reproduction, as well as the ecologically relevant consequences of metabolic changes. In addition, all environmentally relevant exposure routes must be addressed. The available tests do not fulfill these conditions,.

The available information on mammals and birds offer relevant information. The lowest reported NOAEL for traditional endpoints is 2-5 mg/kg bw/d based on slight fetotoxicity or increased liver weights and decreased body weight gain among the maternal treatment group and delayed fetal skeletal ossification. These effects are relevant for the health and the ecological assessment and therefore useful for assessing risks for humans and wildlife. Nevertheless, the additional available information also creates concerns on the capability of these traditional endpoints for assessing the toxicological profile of Hexa to NonaBDE in mammals and other vertebrates.

The immuno-toxicological effects and particularly the delayed neurotoxic effects observed after a single dose require specific attention. Although a quantitative evaluation of these effects in terms of its potential risk for human health and ecosystem is not possible based on the current level of information, the reported observations must be analyzed with care. Certainly, the doses at which the effect have been observed are well above exposure levels in remote areas estimated from current monitoring data for a single congener. However, the effects have been observed for different congeners, and realistic environmental exposure occurs for a mixture of PBDEs. There is not enough information for considering if these effects may be additive or even more than additive in synergistic exposures. The margins between effects observed in the lab and estimated oral exposure levels in the field (based on monitoring data) are not so high when the different isomers/homologues are summed. McDonald (2005) estimated a critical body burden for HexaBDE 153 of 2000 µg/kg lipid based on the NOEL of 0.45 mg/kg reported by Viberg et al 2003 and gives a margin of safety of 7 between this level and the 95 percentile of total PBDE levels in US human populations. It should be noted that HexaBDE 153 concentrations close to these value have been found in several species and geographic sites (see Canada info 2 for a review) and total PBDE concentrations frequently exceed largely this threshold.

The degradation of PBDEs in the environment and biota is a key issue as higher congeners are converted to lower, and possibly more toxic, congeners. This possibility has been demonstrated for debromination of DecaBDE and several c-OctaBDE components (see references above) but the extent to which different PBDEs can be degraded under various conditions, the role of metabolism in addressing the bioaccumulation potential, and the identity of any lower congeners that may be produced, is an active research field. New results will need to be assessed by the POPRC as they appear in refereed literature.

There is an increasing evidence suggesting similar toxicological profiles and therefore, equivalent hazards and concerns, between PBDEs and PCBs, although the mode of action seems to be better categorized by AhR-independent mechanisms, as PBDEs do bind but not activate the AhR-AhR nuclear translocator protein-XRE complex (Peters et al., 2006) and appear capable of up-regulating CYP2B and CYP3A in rats at doses similar to that for non-dioxin-like

PCB153 (Sanders et al., 2005). As the persistence, bioaccumulation potential and long range transport of the c-OctaBDE components are well documented, the confirmation of an equivalent level of hazard for these two groups should be sufficient for confirming a long-range transport associated risk

4. Concluding statement

The evaluation of the human and environmental risk of commercial OctaBDE associated to its potential for long range transport must consider that the commercial product is a mixture of components with different properties and profiles, which may also be released to the environment due to its presence as components of other PBDE commercial products and also produced in the environment by debromination of commercial DecaBDE.

Although the production of c-OctaBDE has ceased in developed countries and there is no information suggesting that the chemical is produced elsewhere; it must be noticed that the product is still present and released from articles in use and during their disposal. Model estimations and measured levels in sewage sludge suggest that current emissions are still significant.

The persistence of the Hexa to NonaBDE is well documented. The main route of degradation is debromination forming other BDEs, also of concern. The potential for certain components in c-OctaBDE to bioaccumulate and also for biomagnification in some trophic chains is also sufficiently documented and confirmed by the good agreement between field observations in monitoring programmes and toxicokinetic studies. Monitoring data in remote areas confirm the potential for long-range transport and at least for some congeners the relevance of atmospheric distribution in this process.

The highest difficulty appears for the estimation of the potential hazard of the commercial mixture and its components. There are traditional ecotoxicological and toxicological studies where no effects have been observed even at unrealistically high concentrations. However, an in-depth assessment of these studies considering in particular the properties and toxicokinetic of PBDE indicates that the test design, exposure conditions and measured endpoints are not appropriate for a sound assessment of these types of chemicals. Thus, the lack of effects reported in those tests should be considered with care. In addition, specific studies have reported particular hazards such as delayed neurotoxicity and immunotoxicity which may be particularly relevant in the assessment of both human health and ecosystem risks.

Based on the existing evidence, it is concluded that the Hexa and HeptaBDE components of the commercial octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

The increasing evidence related to debromination of Octa and Nona BDE into BDEs with POPs properties and considering that under Article 8, paragraph 7(a) of the Convention states that the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the Octa and NonaBDE components of the commercial octabromodiphenyl ether are likely, as a result of LRET, to lead to significant adverse human health and/or environmental effects, such that global action is warranted.

References

Alaee M, Luross J, Sergeant DB,. Muir DCG,. Whittle DM, Solomon K, 1999. Distribution of polybrominated diphenyl ethers in the Canadian environment. Organohalogen Compounds. 40: 347-350.

Allchin CR, Law RJ, Morris S, 1999. Polybrominated diphenylethers in sediments and biota downstream of potential sources in the UK. Environmental Pollution 105: 195-207.

Alonso E, Tapie N, Budzinski H, Tarazona, JV 2006. Calibration of biomagnification model. Kinetic Behaviour Of Several Compounds In Mytilus edulis and Sparus aurata After Oral Exposure. LRI Programme Environment: persistence, bioaccumulation & toxicity. Project No: ECO-1AINIA-1100. Milestone Report.

Bergander L, Kierkegaard A,Sellström U, Widequist U, de Wit C, 1995. Are brominated flame retardants present in ambient air? Poster presentation, 6th Nordic Symposium on Organic Pollutants, Smygehuk, September 17-20.

Breivik K, Wania F, Muir DC, Alaee M, Backus S, Pacepavicius G, 2006. Empirical and modeling evidence of the long-range atmospheric transport of decabromodiphenyl ether. Environ Sci Technol. 40:4612-8.

Breslin WJ, Kirk HD, Zimmer MA, 1989. Teratogenic evaluation of a polybromodiphenyl oxide mixture in New Zealand White rabbits following oral exposure. Fundamental and Applied Toxicology 12:151-157.

Burreau S, Zebuhr Y, Broman D, Ishaq R, 2004. Biomagnification of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) studied in pike (*Esox lucius*), perch (*Perca fluviatilis*) and roach (*Rutilus rutilus*) from the Baltic Sea. Chemosphere 55:1043-52.

Burreau S, Zebuhr Y, Broman D, Ishaq R, 2006. Biomagnification of PBDEs and PCBs in food webs from the Baltic Sea and the northern Atlantic Ocean. Sci Total Environ. 366:659-72

Cheng H, Zhang G, Jiang JX, Li X, Liu X, Li J, Zhao Y, 2007. Organochlorine pesticides, polybrominated biphenyl ethers and lead isotopes during the spring time at the Waliguan Baseline Observatory, northwest China: Implication for long-range atmospheric transport. Atmospheric Environment 41: 4734-47.

Ciparis S, Hale RC, 2005. Bioavailability of polybrominated diphenyl ether flame retardants in biosolids and spiked sediment to the aquatic oligochaete, Lumbriculus variegatus. Environ Toxicol Chem. 24:916-25.

CITI, 1982. The bioaccumulation of compound S512 by carp. Chemical Biotesting Center, CITI, Tokyo.

de Wit CA, Alaee M, Muir DCG, 2006. Levels and trends of brominated flame retardants in the Arctic. Chemosphere 64:209-233

Drouillard KG, Chan S, O'rourke S, Douglas Haffner G, Letcher RJ, 2007. Elimination of 10 polybrominated diphenyl ether (PBDE) congeners and selected polychlorinated biphenyls (PCBs) from the freshwater mussel, Elliptio complanata. Chemosphere. [Epub ahead of print].

Drouillard KG, Fernie KJ, Letcher RJ., Shutt LJ., Whitehead M, Gebink W and Bird DM, 2007. Bioaccumulation and biotransformation of 61 polychlorinated biphenyl and four polybrominated diphenyl ether congeners in juvenile american kestrels (*Falco sparverius*). Environ. Toxicol. Chem. 26:313–324.

EC. 2003. European Union risk assessment report. Diphenyl ether, octabromo derivative. CAS No.: 32536-52-0. EINECS No.: 251-087-9. Risk assessment. Final report, ECB-JRC, Ispra.

Eljarrat E, De La Cal A, Larrazabal D, Fabrellas B, Fernández-Alba AR, Borrull F, Marce M, Barceló D, 2005. Ocurrence of polybrominated diphenylethers, polychlorinated dibenzo-p-dioxins, dibenzofurans and biphenyls in coastal sediments from Spain. Environ. Pollut. 136:493-501.

Elliot JE, Wilson LK, Wakeford B, 2005. Polybrominated diphenyl ether trends in eggs of marine and freshwater birds from British Columbia, Canada 1979-2002. Environ. Sci. Technol. 39:5584-91.

Environment Agency Japan, 1991. Chemicals in the Environment. Report on Environmental Survey and Wildlife Monitoring of Chemicals in F.Y. 1988 & 1989. Office of Health Studies, Department of Environmental Health, Environment Agency Japan. March 1991.

Environment Agency UK, 1997. Report on the Monitoring of Brominated Flame Retardants in the Environment. The Environment Agency, Bath, United Kingdom.

Environment Canada, 2004. Environment Screening Assessment Report on Polybrominated Diphenyl Ethers (PBDEs). Draft for public comments, February 2004.

Environment Canada, 2006. Ecological Screening Assessment Report on Polybrominated Diphenyl Ethers (PBDEs). Environment Canada. June 2006.

Eriksson P, Viberg H, Fischer C, Wallin M, Fredriksson A, 2002. A comparison on developmental neurotoxic effects of hexabromocyclododecane, 2, 2', 4, 4', 5, 5'-hexabromodiphenyl ether (PBDE 153) and 2, 2', 4, 4', 5, 5'-hexachlorobiphenyl (PCB 153). Organohalogen Compounds 57: 389-390.

Evenset A, Christensen GN, Carroll J, Zaborska A, Berger U, Herzke D, Gregor D, 2007. Historical trends in persistent organic pollutants and metals recorded in sediment from Lake Ellasjøen, Bjørnøya, Norwegian Arctic. Environ. Pollut. 146:196-205.

Fernandez MF, Araque P, Kiviranta H, Molina-Molina JM, Rantakokko P, Laine O, Vartiainen T, Olea N, 2007. PBDEs and PBBs in the adipose tissue of women from Spain. Chemosphere 66:377-383.

Fernie KJ, Laird Shutt J, Ritchie IJ, Letcher RJ, Drouillard K, Bird DM, 2006. Changes in the growth, but not the survival, of American kestrels (Falco sparverius) exposed to environmentally relevant polybrominated diphenyl ethers. J Toxicol Environ Health A. 69:1541-54.

Fernie KJ, Mayne G, Shutt JL, Pekarik C, Grasman KA, Letcher RJ, Drouillard K, 2005. Evidence of immunomodulation in nestling American kestrels (Falco sparverius) exposed to environmentally relevant PBDEs. Environ Pollut. 138:485-93.

Gaul S, Von der Recke R, Tomy G, Vetter W, 2006. Anaerobic transformation of a technical brominated diphenyl ether mixture by super-reduced vitamin B12 and dicyanocobinamide. Environ Toxicol Chem. 25:1283-90.

Gerecke, AC, Hartmann PC, Heeb NV, Kohler H-PE, Giger W, Schmid P, Zennegg M, Kohler M, 2005. Anaerobic degradation of decabromodiphenyl ether. Environ. Sci. Technol. 39:1078-1083.

Gevao B, Beg MU, Al-Ghadban AN, Al-Omair A, Helaleh M, Zafar J, 2006. Spatial distribution of polybrominated diphenyl ethers in coastal marine sediments receiving industrial and municipal effluents in Kuwait. Chemosphere. 62:1078-86.

Great Lakes Chemical Corporation. 2001a. Octabromodiphenyl ether: A prolonged sediment toxicity test with Lumbriculus variegatus using spiked sediment with 2% total organic carbon. Final Report. Wildlife International Ltd. Project Number: 298A-112, February 2001.

Great Lakes Chemical Corporation. 2001b. Octabromodiphenyl ether: A prolonged sediment toxicity test with Lumbriculus variegatus using spiked sediment with 5% total organic carbon. Final Report. Wildlife International Ltd. Project Number: 298A-113, February 2001.

Great Lakes Chemical Corporation. 2001c. Effect of octabromodiphenyl oxide on the survival and reproduction of the earthworm, Eisenia fetida. ABC Laboratories, Inc. Report. ABC Study No. 46419, December 2001.

Great Lakes Chemical Corporation. 2001d. Octabromodiphenyl oxide: A toxicity test to determine the effects of the test substance on seedling emergence of six species of plants. Final Report. Wildlife International, Ltd. Project Number: 298-103, August 2001.

Harrad S, Porter L, 2007. Concentrations of polybrominated diphenyl ethers in blood serum from New Zealand. Chemosphere 66:2019-2023.

Hassanin A, Breivik K, Meijer SN, Steinnes E, Thomas GO, Jones KC, 2004. PBDEs in European background soils: levels and factors controlling their distribution. Environmental Science and Technology 38:738-745.

He J, Robrock KR, Alvarez-Cohen L, 2006. Microbial reductive debromination of polybrominated diphenyl ethers (PBDEs). Environ Sci Technol. 40:4429-34.

Isosaari P, Lundebye AK, Ritchie G, Lie O, Kiviranta H, Vartiainen T, 2005. Dietary accumulation efficiencies and biotransformation of polybrominated diphenyl ethers in farmed Atlantic salmon (Salmo salar). Food Addit Contam. 22:829-37.

Kierkegaard A, Asplund L, de Wit CA, McLachlan MS, Thomas GO, Sweetman AJ, Jones KC, 2007. Fate of higher brominated PBDEs in lactating cows. Environ Sci Technol. 41:417-23.

Kodavanti PR, Ward TR, Ludewig G, Robertson LW, Birnbaum LS, 2005. Polybrominated diphenyl ether (PBDE) effects in rat neuronal cultures: 14C-PBDE accumulation, biological effects, and structure-activity relationships. Toxicol Sci. 88:181-92.

Kolic TM, MacPherson KA, Reiner EJ, Ho T, Kleywegt S, Payne M, Alaee M, 2003. Investigation of brominated diphenyl ethers in various land applied materials. Abstract. 5th Annual Workshop on Brominated Flame Retardants in the Environment, August 22-23, 2003, Boston, MA.

Kolic TM, MacPherson KA, Reiner EJ, Ho T, Kleywegt S, Dove A, Marvin C, 2004. Brominated diphenyl ether levels: a comparison of tributary sediments versus biosolid material. Organohalogen Compounds 66: 3830-3835.

Knudsen LB, Gabrielsen GW, Vereault J, Barret R, Utne Skare J, Polder A, Lie E, 2005. Temporal trends of brominated flame retardants, cyclododeca-1,5,9-triene and mercury in eggs offour seabirds species from Northern Norway and Svalbard. SPFO-Report 942/2005.

La Guardia MJ, Hale RC, Harvey E, Mainor TM, Gaylor MO, 2001. Polybrominated diphenyl ethers in land-applied sewage sludge (biosolids). Poster presented at the Society of Environmental Toxicology and Chemistry 22nd Annual Meeting. November 2001.

La Guardia MJ, Hale RC, Harvey E, 2006. Detailed polybrominated diphenyl ether (PBDE) congener composition of the widely used penta-, octa-, and deca-PBDE technical flame-retardant mixtures. Environ Sci Technol. 40:6247-54.

Law RJ, Allchin CR, Morris S, Reed J, 1996. Analysis of brominated flame retardants in environmental samples. DFR No C956H108. Ministry of Agriculture, Fisheries and Food, Directorate of Fisheries Research, Burnham-on Crouch.

Law RJ, Alaee M, Allchin CR, Boon JP, Lebeuf M, Lepom P, Stern GA, 2003. Levels and trends of polybrominated diphenylethers (PBDEs) and other brominated flame retardants in wildlife. Environment International 29:757-770.

Law K, Halldorson T, Danell R, Stern G, Gewurtz S, Alaee M, Marvin C, Whittle M, Tomy G, 2006. Bioaccumulation and trophic transfer of some brominated flame retardants in a Lake Winnipeg (Canada) food web. Environ Toxicol Chem 25:2177–2186 (Erratum in: Environ Toxicol Chem. 2007 26:190).

Lee S-J, Ikonomou MG, Park H, Baek S-Y, Chang Y-S, 2007. Polybrominated diphenyl ethers in blood from Korean incinerator workers and general population Chemosphere 67:489-497.

Lindberg P, Sellström U, Häggberg L, de Wit CA, 2004. Higher brominated PBDEs and hexabromocyclododecane found in eggs of peregrine falcon (*Falco peregrinus*) breeding in Sweden. Environmental Science and Technology 34:93-96.

Luckey FJ, Fowler B, Litten S, 2002. Establishing baseline levels of polybrominated diphenyl ethers in Lake Ontario surface waters. Unpublished manuscript dated 2002/03/01. New York State Department of Environmental Conservation, Division of Water, Albany, NY 12233-3508.

Martínez MA, De la Torre A, Sanz P, Navarro I, Concejero MA, 2006.Ocurrence of brominated flame retardants in sewage sludges from Spain: Higher brominated diphenyl ethers contribution. Organohalogenated compounds 68:1804-1807.

Marvin C, Williams D, Kuntz K, Klawunn P, Backus S, Kolic T, Lucaciu C, MacPherson K, Reiner E, 2007. Temporal trends in polychlorinated dibenzo-p-dioxins and dibenzofurans, dioxin-like PCBs, and polybrominated diphenyl ethers in Niagara river suspended sediments. Chemosphere 67:1808-1815.

McDonald TA, 2005. Polybrominated Diphenylether Levels among United States Residents: Daily Intake and Risk of Harm to the Developing Brain and Reproductive Organs. Integrated Environmental Assessment and Management 1:343-354.

Moon HB, Kannan K, Lee SJ, Choi M, 2007a. Atmospheric deposition of polybrominated diphenyl ethers (PBDEs) in coastal areas in Korea. Chemosphere.66:585-93.

Moon H-B, Kannan K, Lee S-J, Choi M, 2007b. Polybrominated diphenyl ethers (PBDEs) in sediment and bivalves from Korean coastal waters. Chemosphere 66:243-251.

Morf L, Smutny R, Taverna R, Daxbeck H. Selected polybrominated flame retardants PBDE and TBBPA: Substance flow analysis. ENVIRONMENTAL SERIES No. 338, Environmentally hazardous substances. 2002. Swiss Agency for the Environment, Forests and Landscape (SAEFL; now Federal Office for the Environment FOEN), Bern, Switzerland

Norstrom RJ, Simon M, Moisey J, Wakeford B, Weseloh DVC, 2002. Geographical distribution (2000) and temporal trends (1981-2000) of brominated diphenyl ethers in Great Lakes herring gull eggs. Environmental Science and Technology 36:4783-4789.

NICNAS, 2007. Interim Public Health Risk Assessment of Certain PBDE congeners. National Industrial Chemicals Notification and Assessment Scheme
GPO Box 58, Sydney NSW 2001, Australia
OECD, 1994. Selected brominated flame retardants. Risk Reduction Monograph No. 3, OECD Environment Monograph Series No. 102, Paris.

Peterman PH, Orazio CE, Feltz KP, 2003. Sunlight photolysis of 39 mono–hepta PBDE congeners in lipid. Organohalogen Compd. 63:357–360.

Peters AK, Nijmeijer S, Gradin K, Backlund M, Bergman A, Poellinger L, Denison MS, Van den Berg M, 2006. Interactions of polybrominated diphenyl ethers with the aryl hydrocarbon receptor pathway. Toxicol Sci. 92:133-42.

Rayne S, Wan P, Ikonomou M, 2006. Photochemistry of a major commercial polybrominated diphenyl ether flame retardant congener: 2,2',4,4',5,5'-hexabromodiphenyl ether (BDE153). Environ Int. 32:575-85.

Rice CP, Chernyak SM, Begnoche L, Quintal R, Hickey J, 2002. Comparisons of PBDE composition and concentration in fish collected from the Detroit River, MI and Des Plaines River, IL. Chemosphere 49:731-737.

Sanchez-Prado L, Lores M, Llompart M, Garcia-Jares C, Bayona JM, Cela R, 2006. Natural sunlight and sun simulator photolysis studies of tetra- to hexa-brominated diphenyl ethers in water using solid-phase microextraction. J Chromatogr A. 1124:157-66.

Sanders JM, Burka LT, Smith CS, Black W, James R, Cunningham ML. Differential expression of CYP1A, 2B, and 3A genes in the F344 rat following exposure to a polybrominated diphenyl ether mixture or individual components. Toxicol Sci. 2005 Nov;88(1):127-33.

Schmid P, Kohler M, Gujer E, Zennegg M, Lanfranchi M, 2007. Persistent organic pollutants, brominated flame retardants and synthetic musks in fish from remote alpine lakes in Switzerland, Chemosphere, doi:10.1016/j.chemosphere.2006.05.080.

Schuhmacher M, Kiviranta H, Vartiainen T, Domingo JL, 2007. Concentrations of polychlorinated biphenyls (PCBs) and polybrominated diphenyl ethers (PBDEs) in milk of women from Catalonia, Spain. Chemosphere 67:S295-S300.

Sormo EG, Salmer MP, Jenssen BM, Hop H, Baek K, Kovacs KM, Lydersen C, Falk-Petersen S, Gabrielsen GW, Lie E, Skaare JU, 2006. Biomagnification of polybrominated diphenyl ether and hexabromocyclododecane flame retardants in the polar bear food chain in Svalbard, Norway. Environ Toxicol Chem. 25:2502-11.

Stapleton HM, Baker JE, 2003. Debromination of BDE congeners by the common carp (Cyprinus carpio). 5th Annual Workshop on Brominated Flame Retardants in the Environment, August 22–23, Boston, MA.

Stapleton HM, Letcher RJ, Li J, Baker JE, 2004a. Dietary accumulation of polybrominated diphenyl ethers by juvenile carp (Cyprinus *carpio*). Environ Toxicol Chem. 23:1939-1946.

Stapleton HM, Letcher RJ, Baker JE, 2004b. Debromination of polybrominated diphenyl ether congeners BDE 99 and BDE 183 in the intestinal tract of thecommoncarp (*Cyprinus carpio*). Environ. Sci. Technol., 38:1054-1061.

Stapleton HM, Brazil B, Holbrook RD, Mitchelmore CL, Benedict R, Konstantinov A, Potter D, 2006. *In vivo* and *in vitro* debromination of decabromodiphenyl ether (BDE 209) by juvenile rainbow trout and common carp. Environ Sci Technol. 40:4653-8.

Strandberg B, Dodder NG, Basu I, Hites RA, 2001. Concentrations and spatial variations of polybrominated diphenyl ethers and other organohalogen compounds in Great Lakes air. Environ. Sci. Technol. 35:1078-1083.

Thomsen C, Liane VH, Becher G, 2007. Automated solid-phase extraction for the determination of polybrominated diphenyl ethers and polychlorinated biphenyls in serum—application on archived Norwegian samples from 1977 to 2003. J. Chromatogr. B, 846: 252-263.

Toms LM, Harden FA, Symons RK, Burniston D, Furst P, Muller JF, 2007. Polybrominated diphenyl ethers (PBDEs) in human milk from Australia. Chemosphere. Apr 11; [Epub ahead of print].

Tomy GT, Palace VP, Halldorson T, Braekevelt E, Danell R, Wautier K, Evans B, Brinkworth L, Fisk AT, 2004. Bioaccumulation, biotransformation, and biochemical effects of brominated diphenyl ethers in juvenile lake trout (Salvelinus namaycush). Environ Sci Technol. 38:1496-504.

van Beusekom OC, Eljarrat E, Barcelo D, Koelmans AA, 2006. Dynamic modeling of food-chain accumulation of brominated flame retardants in fish from the Ebro River Basin, Spain. Environ Toxicol Chem. 25:2553-60.

Van den Steen E, Covaci A, Jaspers VL, Dauwe T, Voorspoels S, Eens M, Pinxten R, 2007. Accumulation, tissue-specific distribution and debromination of decabromodiphenyl ether (BDE 209) in European starlings (*Sturnus vulgaris*). Environ Pollut. 148:648-653.

Wakeford BJ, Simon MJ, Elliott JE, Braune BM, 2002. Analysis of polybrominated diphenyl ethers (BDEs) in wildlife tissues - Canadian Wildlife Service contributions. Abstract. 4th Annual Workshop on Brominated Flame Retardants in the Environment, June 17-18, 2002, Canada Centre for Inland Waters, Burlington, Ontario.

Wang XM, Ding X, Mai BX, Xie ZQ, Xiang CH, Sun LG, Sheng GY, Fu JM, Zeng EY, 2005. Polybrominated diphenyl ethers in airborne particulates collected during a research expedition from the Bohai Sea to the Arctic. Environ Sci Technol. 39:7803-9.

Wania F, Dugani CB, 2003. Assessing the long-range transport potential of polybrominated diphenyl ethers: a comparison of four multimedia models. Environ Toxicol Chem. 22:1252-61.

Wurl O, Potter JR, Durville C, Obbard JP, 2006. Polybrominated diphenyl ethers (PBDEs) over the open Indian Ocean. Atmospheric Environment 40:5558-65.

Viberg H, Fredriksson A, Jakobsson E, Örn U, Eriksson P, 2001. Neonatal exposure to hexabromo-diphenyl ether (PBDE 153) affects behaviour and cholinergic nicotinic receptors in brain of adult mouse. Abstracts. The Second International Workshop on Brominated Flame Retardants. BFR 2001 Stockholm. May 14-16. Stockholm University, Sweden. p. 275-278.

Viberg H, Fredriksson A, Eriksson P, 2003. Neonatal exposure to polybrominated diphenyl ether (PBDE 153) disrupts spontaneous behaviour, impairs learning and memory, and decreases hippocampal cholinergic receptors in adult mice. Toxicol. Appl. Pharmacol. 192:95-106.

Viberg H, Johansson N, Fredriksson A, Eriksson J, Marsh G, Eriksson P, 2006. Neonatal exposure to higher brominated diphenyl ethers, hepta-, octa-, or nonabromodiphenyl ether, impairs spontaneous behavior and learning and memory functions of adult mice. Toxicol Sci. 92:211-8.

Voorspoels S, Covaci A, Neels H, Schepens P, 2007. Dietary PBDE intake: A market-basket study in Belgium. Environ. Inter. 33:93-97.

Wegmann F, MacLeod M, Scheringer M, 2007. POP Candidates 2007: Model results on overall persistence and long-range transport potential using the OECD Pov & LRTP Screening Tool. Swiss Federal Institute of Technology, http://www.pops.int/documents/meetings/poprc/prepdocs/annexEsubmissions/All%20chemicals%20Switzerland.pdf (OECD Pov & LRTP Screening Tool available at http://www.sust-chem.ethz.ch/downloads).

WHO 1994. Brominated diphenyl ethers. Environmental Health Criteria 162, International Programme on Chemical Safety, WHO, Geneva.

Zhou T, Ross DG, DeVito MJ, Crofton KM, 2001. Effects of short-term in vivo exposure to polybrominated diphenyl ethers on thyroid hormones

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資料　2

残留性有機汚染物質に関するストックホルム条約の新規対象物質を化審法第一種特定化学物質に指定することについて

平成２１年７月２３日

厚生労働省医薬食品局審査管理課化学物質安全対策室

【背景】

1．残留性有機汚染物質に関するストックホルム条約（平成１６年５月発効。以下「ＰＯＰｓ条約」という。）においては、難分解性、生物蓄積性、毒性及び長距離移動性を有する POPs（Persistent Organic Pollutants、残留性有機汚染物質）による人の健康の保護及び環境の保全を図るため、各国が国際的に協調して、条約の対象物質について、製造及び使用を原則禁止する等の措置を講じることとしている（参考１）。我が国においては、平成１７年に国内実施計画を定め、対象物質に関する製造、使用、輸入及び輸出の規制については、化審法、農薬取締法、薬事法、及び外為法に基づき、所要の措置が講じられているところである。化審法においては、現在のＰＯＰｓ条約対象物質のうち、意図的に製造されることのない PCDD 及び PCDF を除いた１０物質について、第一種特定化学物質（以下「一特」という。）に指定し、製造、輸入の許可制（事実上禁止）、使用の制限及び届出制（事実上禁止）等の措置を講じている。

2．ＰＯＰｓ条約における対象物質の追加のための手続きとしては、締約国から提案のあった候補物質について、残留性有機汚染物質検討委員会（以下「ＰＯＰＲＣ」という。）において、締約国等から提供された科学的知見に基づき、条約で定められた手順に基づく検討を行うこととされている（我が国からは、委員として北野大　明治大学教授が第１回より継続的に出席。検討の手順については参考２を参照。）。昨年秋までに、４回のＰＯＰＲＣが開催されており、その結果、締約国会議に対して、９種類の物質について、附属書 A（廃絶）、附属書 B（制限）又は附属書 C（非意図的放出の削減）へ追加する旨の勧告を行うことが決定された。

3．本年５月に開催された第４回締約国会議においては、上記勧告を踏まえ、当該９種類の物質を附属書に追加することが検討された。その結果、各物質について、参考３のとおり附属書に新たに追加することが決定された。これら物質については、今後、条約の下で、製造、使用等を廃絶・制限する措置等が講じられることとなる（改正される附属書の発効は、国連事務局による各国への通報から１年後）。

【化審法による対応】

4．今回附属書に追加されることとなった化学物質については、①ＰＯＰｓとしての要件（参考４）を満たすことがＰＯＰＲＣにより既に科学的に評価されており（別添１～９を参照）、これらの要件は化審法の一特と同様に、分解性、蓄積性並びに人等への毒性を考慮したものであること、②工業化学品として意図的に製造される可能性がある物質であることから、下表のとおり、速やかに化審法の一特に指定し、現在のＰＯＰｓ条約対象物質と同様に、関係法令とも連携しつつ、原則、これら物質の製造・使用等を禁止するための所要の措置を講ずることとしたい。

５．　なお、これら物質のうち「PFOSとその塩及びPFOSF」については、日本としても、条約で認められた範囲で我が国に必須の特定の用途について適用除外の登録等を行う予定であり、化審法等の国内担保法体系において、その用途の内容及び管理のために必要な措置等について検討する必要がある。

POPs条約への新規追加に伴い化審法第一種特定化学物質へ指定を行う物質(案)

No.	化学物質名	CAS番号	化審法官報公示整理番号
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	1763-23-1 2795-39-3* 4021-47-0* 29457-72-5* 29081-56-9* 70225-14-8* 56773-42-3* 251099-16-8*	2-1595 2-2810
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)	307-35-7	2-2803
3	ペンタクロロベンゼン	608-93-5	3-76
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)	319-84-6	3-2250 9-1652
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)	319-85-7	3-2250 9-1652
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)	58-89-9	3-2250 9-1652
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)	143-50-0	
8	ヘキサブロモビフェニル	36355-01-8	
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)	40088-47-9**	3-61
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)	32534-81-9**	
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)	68631-49-2*** 207122-15-4***	3-2845
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)	446255-22-7*** 207122-16-5***	3-3716****

*ペルフルオロオクタンスルホン酸塩の例

**商業用ペンタブロモジフェニルエーテルに含まれる代表的な異性体

***商業用オクタブロモジフェニルエーテルに含まれる代表的な異性体

****ジフェニル＝エーテルの臭素化物(Br＝7～9)として

参考１　ＰＯＰｓ条約の概要
参考２　新規ＰＯＰｓの追加フロー
参考３　第４回締約国会議において決定された事項
参考４　ＰＯＰｓ条約附属書Ｄに規定されている情報の要件及び選別のための基準
別添１～９　ＰＯＰＲＣにおいて作成された危険性の概要（Risk Profile）

（参考１）残留性有機汚染物質に関するストックホルム条約（POPs条約）の概要

１．目　的

リオ宣言第15原則に掲げられた予防的アプローチに留意し、毒性、難分解性、生物蓄積性及び長距離移動性を有するPOPs（Persistent Organic Pollutants、残留性有機汚染物質）から、人の健康の保護及び環境の保全を図る。

２．各国が講ずべき対策

①PCB等9物質の製造、使用の原則禁止及び原則制限（DDTのみ）
②ダイオキシン、PCB等4物質の非意図的生成物質の排出の削減
③POPsを含む在庫・廃棄物の適正管理及び処理
④これらの対策に関する国内実施計画の策定
⑤その他の措置

- 条約対象12物質※1と同様の性質を持つ有機汚染物質の製造・使用を防止するための措置
- POPsに関する調査研究、モニタリング、情報提供、教育等
- 途上国に対する技術・資金援助の実施

３．条約の発効

平成16年5月17日発効（日本は平成14年8月30日に締結済）。平成21年5月1日現在162ヶ国(+EC)が締結。

４．条約発効後の動き

対象物質追加の検討を行うPOPs検討委員会会合を、平成17～20年の各年11月に開催。平成21年5月に開催されたCOP4において新たに9物質※2の追加が決定された。

５．我が国の対応

○　対象物質の製造・使用禁止等については、化審法、農薬取締法等で措置。

○　関係省庁連絡会議（議長は環境保健部長）において国内実施計画を作成し、平成17年6月、地球環境保全に関する関係閣僚会議にて了承。

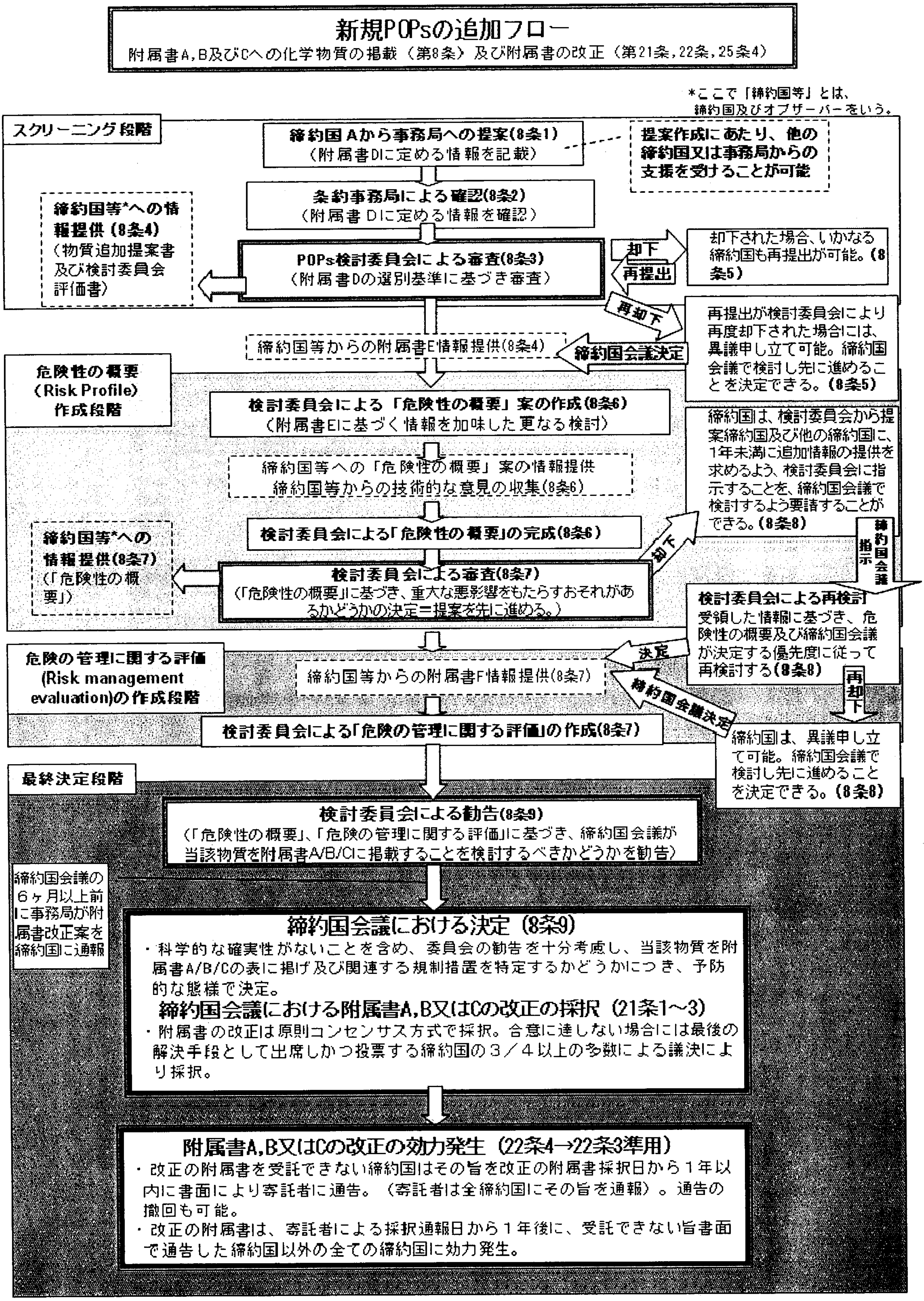
○　我が国の主導により東アジアPOPsモニタリング事業を実施。

○　POPs検討委員会に北野大　明治大学教授を、条約有効性評価のための調整グループ及び地域組織グループに柴田康行　国立環境研究所化学領域長を派遣。

※1　対象物質：
アルドリン、ディルドリン、エンドリン、クロルデン、ヘプタクロル、トキサフェン、マイレックス、ヘキサクロロベンゼン、PCB、DDT、ダイオキシン・ジベンゾフラン

※2　COP4において追加された物質：
クロルデコン、リンデン、テトラ・ペンタブロモジフェニルエーテル、ヘキサブロモビフェニル、ペルフルオロオクタンスルホン酸及びその塩、パーフルオロオクタンスルホン酸フルオリド（PFOS及びその塩、PFOSF）、ペンタクロロベンゼン、ヘキサ・ヘプタブロモジフェニルエーテル、α-ヘキサクロロシクロヘキサン（α-HCH）、β-ヘキサクロロシクロヘキサン（β-HCH）

（参考２）新規ＰＯＰｓの追加フロー



新規POPsの追加フロー

附属書A,B及びCへの化学物質の掲載（第8条）及び附属書の改正（第21条，22条，25条4）

*ここで「締約国等」とは、締約国及びオブザーバーをいう。

スクリーニング段階

締約国Aから事務局への提案(8条1)
（附属書Dに定める情報を記載）

提案作成にあたり、他の締約国又は事務局からの支援を受けることが可能

条約事務局による確認(8条2)
（附属書Dに定める情報を確認）

締約国等*への情報提供(8条4)
（物質追加提案書及び検討委員会評価書）

POPs検討委員会による審査(8条3)
（附属書Dの選別基準に基づき審査）

却下

再提出

却下された場合、いかなる締約国も再提出が可能。(8条5)

再却下

再提出が検討委員会により再度却下された場合には、異議申し立て可能。締約国会議で検討し先に進めることを決定できる。(8条5)

締約国会議決定

締約国等からの附属書E情報提供(8条4)

危険性の概要（Risk Profile）作成段階

検討委員会による「危険性の概要」案の作成(8条6)
（附属書Eに基づく情報を加味した更なる検討）

締約国等への「危険性の概要」案の情報提供
締約国等からの技術的な意見の収集(8条6)

検討委員会による「危険性の概要」の完成(8条6)

締約国等*への情報提供(8条7)
（「危険性の概要」）

検討委員会による審査(8条7)
（「危険性の概要」に基づき、重大な悪影響をもたらすおそれがあるかどうかの決定＝提案を先に進める。）

却下

締約国は、検討委員会から提案締約国及び他の締約国に、1年未満に追加情報の提供を求めるよう、検討委員会に指示することを、締約国会議で検討するよう要請することができる。(8条8)

締約国会議指示

検討委員会による再検討
受領した情報に基づき、危険性の概要及び締約国会議が決定する優先度に従って再検討する(8条8)

決定

再却下

締約国は、異議申し立て可能。締約国会議で検討し先に進めることを決定できる。(8条8)

締約国会議決定

危険の管理に関する評価(Risk management evaluation)の作成段階

締約国等からの附属書F情報提供(8条7)

検討委員会による「危険の管理に関する評価」の作成(8条7)

最終決定段階

検討委員会による勧告(8条9)
（「危険性の概要」、「危険の管理に関する評価」に基づき、締約国会議が当該物質を附属書A/B/Cに掲載することを検討するべきかどうかを勧告）

締約国会議の6ヶ月以上前に事務局が附属書改正案を締約国に通報

締約国会議における決定（8条9）

・科学的な確実性がないことを含め、委員会の勧告を十分考慮し、当該物質を附属書A/B/Cの表に掲げ及び関連する規制措置を特定するかどうかにつき、予防的な態様で決定。

締約国会議における附属書A,B又はCの改正の採択（21条1～3）

・附属書の改正は原則コンセンサス方式で採択。合意に達しない場合には最後の解決手段として出席しかつ投票する締約国の３／４以上の多数による議決により採択。

附属書A,B又はCの改正の効力発生（22条4→22条3準用）

・改正の附属書を受託できない締約国はその旨を改正の附属書採択日から１年以内に書面により寄託者に通告。（寄託者は全締約国にその旨を通報）。通告の撤回も可能。

・改正の附属書は、寄託者による採択通報日から１年後に、受託できない旨書面で通告した締約国以外の全ての締約国に効力発生。

（参考３）第４回締約国会議において決定された事項

〇附属書Aへの追加

物質名	主な用途	決定された主な規制内容	※
テトラブロモジフェニルエーテル、ペンタブロモジフェニルエーテル	プラスチック難燃剤	・製造・使用等の禁止 （以下の用途を除外する規定あり） -当該物質を含有する製品のリサイクル	9,10
クロルデコン CAS No:143-50-0	農薬	・製造・使用等の禁止	7
ヘキサブロモビフェニル CAS No:36355-01-8	プラスチック難燃剤	・製造・使用等の禁止	8
リンデン（γ－ＨＣＨ） CAS No:58-89-9	農薬	・製造・使用等の禁止 （以下の用途を除外する規定あり） -アタマジラミ、疥癬の医薬品用の製造と使用	6
α－ヘキサクロロシクロヘキサン CAS No:319-84-6	リンデンの副生物	・製造・使用等の禁止	4
β－ヘキサクロロシクロヘキサン CAS No:319-85-7	リンデンの副生物	・製造・使用等の禁止	5
ヘキサブロモジフェニルエーテル、ヘプタブロモジフェニルエーテル	プラスチック難燃剤	・製造・使用等の禁止 （以下の用途を除外する規定あり） -当該物質を含有する製品のリサイクル	11,12

〇附属書Bへの追加

物質名	主な用途	決定された主な規制内容	※
ペルフルオロオクタンスルホン酸(PFOS)とその塩、ペルフルオロオクタンスルホン酸フルオリド（PFOSF） CAS No: 1763-23-1 CAS No: 307-35-7	撥水撥油剤、界面活性剤	・製造・使用等の禁止 （以下の目的・用途を除外する規定あり） -写真感光材料 -半導体用途 -フォトマスク -医療機器 -金属メッキ -泡消火剤 -カラープリンター用電気電子部品 -医療用CCDカラーフィルター　など	1,2

〇附属書A及びCへの追加

物質名	主な用途	決定された主な規制内容	※
ペンタクロロベンゼン CAS No: 608-93-5	農薬	・製造・使用等の禁止 ・非意図的生成による排出の削減	3

（注意）上記の表中の情報は省略・簡略化しているため、規制内容の詳細については、条約事務局のホームページ（http://www.pops.int/）から会議文書を御確認いただきたい。

※２ページに記載の物質リストとの対応。

（参考４）ＰＯＰｓ条約附属書Ｄに規定されている情報の要件及び選別のための基準

ＰＯＰＲＣでは、締約国から提案のあった化学物質ごとに、附属書Ｄに定められた選別のための基準（下記を参照）に基づき審査を実施後、附属書Ｅに沿って、これら情報を更に考慮、評価した上で、当該化学物質が、長距離にわたる自然の作用による移動の結果として、世界的規模の行動を正当化するようなヒトの健康又は環境に対する重大な悪影響をもたらすかどうかの評価を行うため、危険性の概要（Risk Profile）の作成が行われる。

化学物質の特定	商品名、商業上の名称、別名、ケミカル・アブストラクツ・サービス（ＣＡＳ）登録番号、国際純正・応用化学連合（ＩＵＰＡＣ）の名称その他の名称
	構造（可能な場合には異性体の特定を含む。）及び化学物質の分類上の構造
残留性（次のいずれか）	化学物質の水中における半減期が２ヶ月を超えること、土中における半減期が６ヶ月を超えること又は堆積物中における半減期が６ヶ月を越えることの証拠
	この条約の対象とすることについての検討を正当とする十分な残留性を化学物質が有することの証拠
生物蓄積性（次のいずれか）	化学物質の水生種の生物濃縮係数若しくは生物蓄積係数が五千を超えること又はこれらの資料がない場合にはオクタノール／水分配係数の常用対数値が五を越えることの証拠
	化学物質に他に懸念される理由（例えば、他の種における高い生物蓄積性、高い毒性、生態毒性）があることの証拠
	化学物質の生物蓄積の可能性がこの条約の対象とすることについての検討を正当とするのに十分であることを示す生物相における監視に基づく資料
長距離にわたる自然の作用による移動の可能性（次のいずれか）	化学物質の放出源から離れた地点における当該化学物質の潜在的に懸念すべき測定の水準
	化学物質が別の環境に移動した可能性とともに、大気、水又は移動性の種を介して長距離にわたり自然の作用により移動した可能性を示す監視に基づく資料
	化学物質がその放出源から離れた地点における別の環境に移動する可能性とともに、大気、水又は移動性の種を介して長距離にわたり自然の作用により移動する可能性を示す環境運命の性質又はモデルによる予測結果。主に大気中を移動する化学物質については、大気中における半減期が二日を超えるべきである。
悪影響（次のいずれか）	この条約の対象となる化学物質とすることについての検討を正当とする人の健康又は環境に対する悪影響を示す証拠
	人の健康又は環境に対する損害の可能性を示す毒性又は生態毒性の資料

資料 3－1

化学物質の審査及び製造等の規制に関する法律に基づく審査状況について

平成20年度第6回以降の薬事・食品衛生審議会薬事分科会化学物質安全対策部会化学物質調査会における化学物質の審査及び製造等の規制に関する法律に基づき行われた新規化学物質及び既存化学物質の審査結果については、以下のとおり。なお、平成20年度第5回までの審査結果については、前回までの化学物質安全対策部会で報告済み。

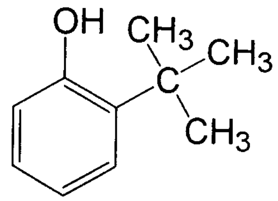
	審議物質数		第一種監視化学物質とされた物質の数	第二種監視化学物質とされた物質の数	
	新規化学物質	既存化学物質		新規化学物質	既存化学物質
平成20年度第6回	80	3	－	3	2
平成20年度第7回	45	－	－	3	－
平成20年度第8回	34	2	－	1	1
平成20年度第9回	21	－	－	1	－
平成20年度第10回	72	－	－	4	－
平成21年度第1回	50	－	－	2	－
平成21年度第2回	26	－	－	3	－
合計	328	5	0	17	3

資料　３－２

化学物質の審査及び製造等の規制に関する法律に基づく既存化学物質の審査の状況について(物質ごとの審議の概要)

既存化学物質審査シート

官報公示整理番号	3-503	CAS No.	88-18-6

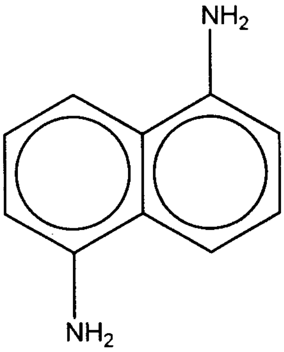
判定結果	人健康影響　第二種監視化学物質相当
名称構造式等	名　称：2－*tert*－ブチルフェノール 
用途	中間物、洗剤等　※化学物質の製造・輸入量に関する実態調査（平成１６年実績）
外観	無色透明液体
分解性	難分解性
蓄積性	高濃縮性でない
Ames	陰性 純度 99.97%．溶媒（DMSO－溶解）． TA98，TA100，TA1535，TA1537，WP2 uvrA. 5000μg/plate まで実施した用量設定試験結果を参考に以下の濃度まで実施． （本試験Ⅰ、Ⅱ） －S9mix 群：200μg/plate（TA98，TA100, TA1535, TA1537：100μg/plate 以上で菌の生育阻害、WP2uvrA：最高用量で菌の生育阻害） ＋S9mix 群：200μg/plate（TA100，TA1535：100μg/plate 以上で菌の生育阻害、TA98，TA1537，WP2uvrA：最高用量で菌の生育阻害）
染色体異常	陽性 D20 値＝0.022mg/mL（＋S9mix 群：構造異常） ＋S9mix 群で構造異常及び数的異常の誘発 純度 99.97%．溶媒（DMSO－溶解）．CHL/IU. 0.14mg/mL（10mM）まで実施した細胞増殖抑制試験の結果を参考に以下の濃度まで実施． －S9mix 群：0.12mg/mL（細胞毒性のため 0.10mg/mL まで観察） ＋S9mix 群：0.02mg/mL（細胞毒性のため 0.01mg/mL まで観察）

28 日間反復投与	投与方法	強制経口投与　溶媒：オリブ油
	純度	99.97%
	用量	4 用量(4, 20, 100, 500 mg/kg/day)
	死亡	なし
	NOEL	20mg/kg/day
	推定根拠	一般状態（流涎：100 以上♂♀）
	他の毒性	一般状態（歩行失調：500♂♀、自発運動↓：500♀） 相対重量（肝↑：500♂♀）
	回復性	問題なし

他の試験	“Elevated susceptibility of newborn as compared with young rats to 2-tert-butylphenol and 2,4-di-tert-butylphenol toxicity.”, Hirata-Koizumi M, Hamamura M, Furukawa H, Fukuda N, Ito Y, Wako Y, Yamashita K, Takahashi M, Kamata E, Ema M, Hasegawa R., Congenit Anom (Kyoto). Dec;45(4):146-153, (2005) SD ﾗｯﾄ 強制経口（20, 60, 200 mg/kg/day）新生児 18 日間（生後 4-21 日） 純度 99.97% NOAEL：20 mg/kg/day 一般状態（自発運動↓：60 以上♂200♀、歩行失調・呼吸深大・筋力↓：200♂♀） 体重↓：200♂♀ 血液生化学的検査（GTP↑：200♂♀、TP↑：200♂） 相対重量（肝：60 以上♀200♂） 組織学的所見（肝ー小葉中心性肝細胞肥大［軽微］：60 以上♀200♂）
人健康影響判定根拠	Ames 試験は陰性であるが染色体異常試験は陽性であり、NOEL20mg/kg/day であることから第二種監視化学物質相当。
備考	

既存化学物質審査シート

官報公示整理番号	4-323	CAS No.	2243-62-1

判定結果	人健康影響　第二種監視化学物質相当 生 態 影 響　第三種監視化学物質相当
名称構造式等	名　称：１，５－ジアミノナフタレン 
用途	－
外観	灰紫色結晶性粉末
分解性	難分解性
蓄積性	高濃縮性でない
人健康影響の毒性情報	【 “Bioassay of 1,5-naphthalenediamine for possible carcinogenicity.”, National Toxicology Program (NTP), Natl Cancer Inst Carcinog Tech Rep Ser, 143:1-123 (1978) より引用 】 発がん性試験 Fischer 344 ラット(0.05, 0.1%〈103 週混餌投与〉) 106～107 週まで観察、純度約 89-90% がん原性：♀であり(陰核腺、子宮) ♀：子宮―内膜間質ポリープ・肉腫(0.05%以上)、陰核腺―腺腫・癌(0.1%) B6C3F1 マウス(0.1, 0.2%〈103 週混餌投与〉) 105～106 週まで観察、純度約 89-90% がん原性：あり[♂(甲状腺)、♀(甲状腺、肝、肺)] ♂♀：甲状腺―乳頭状腺腫・濾胞細胞腺腫・乳頭状嚢胞腺腫(0.1%以上) ♀：肝―肝細胞癌、肺―細気管支肺胞上皮腺腫(0.1%以上)、 甲状腺―C 細胞癌(0.2%)

【IARC Monographs on the evaluation of the carcinogenic risk of chemicals to humans Vol:27, 127-132 (1982)より引用】

発がん性試験【NTPによる発がん性試験を引用、再評価】

B6C3F1 マウス(0.1%, 0.2%〈103 週混餌投与〉) 105-106 週観察、純度約 89%以上

甲状腺—濾胞細胞腺腫・乳頭状腺腫・乳頭状嚢胞腺腫:0.1%以上♂♀、甲状腺—C 細胞癌、肝—肝細胞癌、肺—細気管支肺胞上皮腺腫・癌:0.1%以上♀

Fischer 344 ラット (0.05%, 0.1%〈103 週混餌投与〉) 106-107 週観察、純度約 89%以上

陰核腺—腺腫・癌:0.05%以上♀

※IARCの作業部会では、ラットの試験については、陰核腺腫瘍はわずかな変化であり、組織学的検査は肉眼的に異常がみられた場合のみ実施と言及し、ラットの試験は評価に値しない“inadequate for evaluation”と記載。

反復投与毒性(用量設定試験)

Fischer 344 ラット(3%まで (混餌投与)) 8 週間

死亡:0.3%以上、体重↓、0.1%以下は異常なし。

B6C3F1 マウス(3%まで (混餌投与)) 8 週間

死亡:0.3%以上、体重↓、0.2%以下は異常なし。

変異原性試験

Ames 試験(TA100、-S9mix):陽性

発癌性に対する評価:実験動物に限定的な証拠”limited evidence”あり

(There is limited evidence for the carcinogenicity of 1,5-naphthalenediamine in experimental animals.)

[IARC. Monographs on the Evaluation of the Carcinogenic Risk of Chemicals to Man. Geneva: World Health Organization, International Agency for Research on Cancer, 1972-PRESENT. (Multivolume work)., p. S7 67 (1987)

発癌性に対する証拠の程度 “Degree of evidence for carcinogenicity”

Human:適切なデータなし”no adequate data”

Animal: 限定的な証拠”limited evidence”

総合評価”overall evaluation”

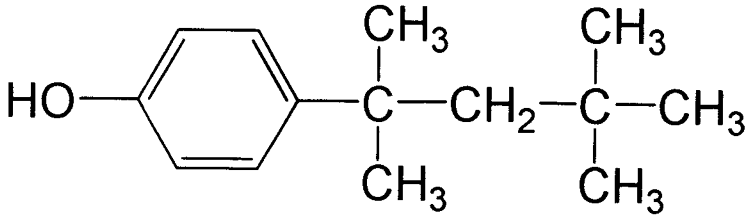
Group 3: 『ヒトに発がん性を示すとしては分類できない(Not Classifiable as to its Carcinogenic) 』.

	【"Reproducibility of Microbial Mutagenicity Assays:2. Testing of Carcinogens and Noncarcinogens in Salmonella Typhimurium and Escherichia Coli", Dunkel,Vc, Zeiger,E, Brusick,D, Mccoy,E, Mcgregor,D, Mortelmans,K, Rosenkranz, Hs, and Simmon,Vf; Environ. Mol. Mutagen., 7(Suppl. 5):1-248, (1985)より引用】 Ames 試験：陽性 純度 96%以上、溶媒：DMSO、アセトン 菌株：TA98, TA100, TA1535, TA1537, TA1538, WP2 uvra +: With metabolic activation -: Without metabolic activation 溶媒：DMSO ・ TA100 -/+群で陽性(1～1000 μg/plate) ・ TA1537 -/+群で陽性(3.3～3333.3 μg/plate) ・ TA98 +群で陽性(1～1000, 3.3～3333.3 μg/plate) ・ TA1538 +群で陽性(3.3～3333.3 μg/plate) ・ TA1535, WP2 uvra -/+群で陰性(1～1000, 3.3～3333.3 μg/plate) 溶媒：アセトン ・TA98, TA100, TA1535, TA1537, TA1538, WP2 uvra -/+群で陰性(0.3～333.3 μg/plate) 【" Salmonella mutagenicity tests: V. Results from the testing of 311 chemicals.", Zeiger E et. al., Environ Mol Mutagen, 19 (Suppl. 21): 2-141, (1992)より引用】 変異原性試験 Ames 試験(TA100、TA98)：陽性 純度記載なし -/+S9mix, 10～3333 μg/plate
人健康影響判定根拠	Ames 試験が陽性であり、ラット、マウス共に発がん性が示されたことから、継続的に摂取される場合人の健康を損なうおそれの疑いがあるため、第二種監視化学物質相当。
藻類生長阻害試験	生物種： *Pseudokirchneriella subcapitata* 試験法：化審法 TG（2006） 培養方式：振とう培養 純度：98.5 % 試験濃度：設定濃度 0.046、0.10、0.22、0.46、1.0、2.2、4.6、10 mg/L 実測濃度 0.024、0.075、0.18、0.34、0.80、1.7、3.2、6.4 mg/L（幾何平均値） 助剤：なし 72hEC50（実測値に基づく）=1.8 mg/L 72hNOEC（実測値に基づく）=0.34 mg/L ①試験溶液が着色していたため、遮光影響を推定するために試験溶液量を半分(50 ml)に減じた追加試験を行っているが、毒性値は 72hEC50（実測値に基づく）=1.5 mg/L であり、通常の試験とほぼ同じであったことから、試験実施者は被験物質による遮光影響は大きくないと判断した。
ミジンコ急性遊泳阻害試験	生物種：オオミジンコ *Daphnia magna* 試験法：化審法 TG 試験方式：半止水式、24 時間後に換水 純度：98.5 % 試験濃度：設定濃度 0.46、0.68、1.0、1.5、2.2、3.2、4.6、6.8 mg/L 実測濃度 0.45、0.68、0.99、1.5、2.2、3.3、4.6、6.6 mg/L（幾何平均値） 助剤：なし 48hEC50（実測値に基づく）=3.8 mg/L

魚類急性毒性試験	生物種：ヒメダカ *Oryzias latipes* 試験法：化審法 TG 試験方式：半止水式、24 時間毎に換水 純度：98.5 % 試験濃度：設定濃度 5.6、7.5、10、13、18、24、32、42 mg/L 実測濃度 5.7、7.2、9.4、12、17、22、30、38 mg/L（幾何平均値） 助剤：なし 96hLC50（実測値に基づく）= 17 mg/L また、以下の濃度群において以下のような毒性症状が認められた。 12mg/L 群：遊泳異常（48hr 1/10、72hr 10/10、96hr 9/9） 17 mg/L 群：遊泳異常+外見異常（72hr 1/10、96hr 1/6） 遊泳異常（48hr 3/10、72hr 9/10、96hr 5/6）
生態影響判定根拠	芳香族アミンを構造中に有し、かつミジンコ急性遊泳阻害試験において 48hEC50=3.8 mg/L、藻類生長阻害試験において 72hEC50=1.8mg/L であることから、第三種監視化学物質相当。
備考	水溶解度：40 mg/L（20℃） 蒸気圧：1.73×10^{-8} mmHg（20℃）

既存化学物質審査シート

官報公示整理番号	3-503	CAS No.	140-66-9

判定結果	人健康影響　第二種監視化学物質相当 生態影響　第三種監視化学物質相当【平成18年7月18日告示済み】
名称構造式等	名　称：*p-tert*-オクチルフェノール 
用途	３－５０３として中間物、合成樹脂、接着剤、添加剤（ゴム用、油用、紙用）、洗剤等 ※化学物質の製造・輸入量に関する実態調査（平成１６年実績）
外観	白色結晶状固体
分解性	難分解性
蓄積性	高濃縮性でない
Ames	陰性 純度≧97%．溶媒（DMSO－溶解）．プレート法． TA98, TA100, TA1535, TA1537, WP2uvrA. 5000μg/plate まで実施した用量設定試験の結果を参考に、以下の濃度まで実施． （本試験Ⅰ） －S9mix 群：50μg/plate（TA1535, TA1537：25μg/plate 以上で菌の生育阻害） （TA98, TA100：最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA：最高用量で菌の生育阻害） ＋S9mix 群：200μg/plate（TA98, TA100, TA1535, TA1537：最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA） （本試験Ⅱ） －S9mix 群：50μg/plate（TA1537：25μg/plate 以上で菌の生育阻害） （TA98, TA100, TA1535：最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA：最高用量で菌の生育阻害） ＋S9mix 群：200μg/plate（TA1537：100μg/plate 以上で菌の生育阻害） （TA98, TA100, TA1535：最高用量で菌の生育阻害） 2000μg/plate（WP2uvrA：最高用量で菌の生育阻害）
染色体異常	陰性 純度≧97%．溶媒（DMSO－溶解）．CHL/IU. 0.1mg/mL まで実施した細胞増殖抑制試験の結果を参考に、以下の濃度まで実施． －S9mix 群：0.005mg/mL（細胞毒性のため、0.0025mg/mL まで観察） ＋S9mix 群：0.04mg/mL 24 時間処理群；0.016mg/mL（細胞毒性のため、0.008mg/mL まで観察） 48 時間処理群：0.016mg/mL（細胞毒性のため、0.008mg/mL まで観察）

28 日間反復投与	投与方法	強制経口投与　溶媒：オリブ油
	純度	98.24%
	用量	3 用量(15, 70, 300 mg/kg/day)
	死亡	予備試験（500♀：1/2、1000♂：1/2、1000♀：2/2）
	NOEL	15 mg/kg/day

	推定根拠	一般状態（流涎：70以上♂♀） 血液生化学的検査(A/G↓：70以上♀)
	他の毒性	体重↓（300♂） 摂水量↑（300♂♀） 一般状態（自発運動量↓：300♂） 血液生化学的検査（Na↑：300♂♀、Alb↓・K↓：300♂、BUN↑・Cho↓・TG↑：300♀） 尿検査（尿比重↓・尿量↑・Na↓・Cl↓：300♂♀） 相対重量（腎↑:300♂♀、肝↑：300♀） 組織学的所見（腎－尿細管再生像：300♂♀）
	回復性	問題なし

人健康影響判定根拠	Ames試験及び染色体異常試験は陰性であるが、NOEL 15mg/kg/dayであることから第二種監視化学物質相当。
備考	

参考資料　1

化学物質の審査及び製造等の規制に関する法律における第一種特定化学物質の取扱いについて

1．第一種特定化学物質の特性

難分解性：自然的作用による化学的変化を生じにくい
高蓄積性：生物の体内に蓄積されやすい
長期毒性：継続的に摂取される場合に人の健康を損なうおそれがある、又は高次捕食動物の生態・生育に支障を及ぼすおそれがある)

2．第一種特定化学物質(政令指定)

（１）ポリ塩化ビフェニル
（２）ポリ塩化ナフタレン（塩素数が３以上のものに限る。）
（３）ヘキサクロロベンゼン
（４）アルドリン
（５）ディルドリン
（６）エンドリン
（７）ＤＤＴ
（８）クロルデン類
（９）ビス（トリブチルスズ）＝オキシド
（１０）Ｎ，Ｎ’－ジトリル－パラ－フェニレンジアミン、Ｎ－トリル－Ｎ’－キシリル－パラ－フェニレンジアミン又はＮ，Ｎ’－ジキシリル－パラ－フェニレンジアミン
（１１）２，４，６－トリ－ターシャリ－ブチルフェノール
（１２）トキサフェン
（１３）マイレックス
（１４）ジコホル
（１５）ヘキサクロロブタ－１，３－ジエン
（１６）２－（２Ｈ－１，２，３－ベンゾトリアゾール－２－イル）－４，６－ジ－ｔｅｒｔ－ブチルフェノール

3．第一種特定化学物質に対する規制措置

（１）製造・輸入の許可制（法第６条～第１２条）
　経済産業大臣による許可
（２）政令で指定した製品の輸入禁止（法第１３条）
（３）特定の用途以外での使用禁止（法第１４条及び第１５条）
　平成２１年改正により、使用の制限に関してストックホルム条約との整合化
（４）基準適合義務（法第１７条）
　平成２１年の法改正により、第一種特定化学物質等の取扱いに係る技術上の基準の遵守義務が新設
（５）表示義務（改正化審法第１７条の２）
　平成２１年の法改正により、環境汚染防止のための措置等に関する表示義務が新設

参考資料　2

既存の第一種特定化学物質に関する毒性評価一覧

物質名	ﾎﾟﾘ塩化ﾋﾞﾌｪﾆﾙ(PCB)	ﾎﾟﾘ塩化ﾅﾌﾀﾚﾝ	ﾍｷｻｸﾛﾛﾍﾞﾝｾﾞﾝ	ｱﾙﾄﾞﾘﾝ	ﾃﾞｨﾙﾄﾞﾘﾝ	ｴﾝﾄﾞﾘﾝ	DDT	ｸﾛﾙﾃﾞﾝ(ｸﾛﾙﾃﾞﾝ類)	ﾍﾌﾟﾀｸﾛﾙ(ｸﾛﾙﾃﾞﾝ類)	ﾋﾞｽ(ﾄﾘﾌﾞﾁﾙｽｽﾞ)=ｵｷｼﾄﾞ
指定年月日	S49.6.7	S54.8.14	S54.8.14	S56.10.2	S56.10.2	S56.10.2	S56.10.2	S61.9.17	S61.9.17	H1.12.27
慢性毒性	［ラット雄　混餌］ 100ppm　肝重量増加	［マウス］ 肝細胞の壊死、変性等、間質の線維化等の肝障害 肝硬変様の非可逆的変化の可能性				［ラット　混餌］ 雄50ppm,雌25ppm以上で死亡率の上昇 50ppm以上で外部刺激に対する感受性の亢進、時に痙攣 25ppm以上の死亡動物には脳、肝、腎及び副腎に、50ppm以上の生存動物には肝臓に、それぞれ瀰漫性変性	［ラット　混餌］ 400ppm以上で神経症状、用量相関性のある死亡率の上昇 すべての投与群（100～800ppm）で肝障害を示す病理所見	［マウス　経口］ 12.5ppmでGOT,GPTの異常 5,12.5ppmで肝腫大、雄で肝細胞変性、壊死 ［ラット　経口］ 25ppmで肝腫大、雄では肝細胞壊死 ［イヌ　経口］ 15,30ppmでTTT,Alpの異常、用量依存の肝重量増加 30ppmで肝相対重量増加と肝細胞の変化 他に甲状腺への影響	［ラット　混餌］ 45ppmで肝障害と認められる肝細胞の組織学的変化 ［ラット　経口］ 5mg/kgで肝、腎及び脾臓に病理所見他に甲状腺への影響	［ラット　経口］ 3～12mg/kgで胸腺重量低下。 6mg/kg以上で副腎重量の増加 ［ラット　混餌］ 80mg/kgで貧血症状、甲状腺重量の低下 100ppm以上で出血傾向胸腺相対重量減少、副腎相対重量の増加 300ppmで死亡率増加、るい痩、貧血症状 50ppmで体重減少、貧血症状、甲状腺重量減少、副腎重量増加、ﾘﾝﾊﾟ球減少等 25ppm以上で体重増加抑制、出血傾向、血液凝固時間の延長 80ppmでﾘﾝﾊﾟ球数減少、胸腺重量減少、血清IgGの減少とIgMの増加
生殖能及び後世代に及ぼす影響	［マウス　混餌］ 500ppmで、F2で催奇形作用は否定できず		［ラット］ 妊娠率低下、児動物生存率及び体重の低下		［ラット　混餌］ 0.24ppm以上で妊娠率低下					
催奇形性	［ラット　混餌］ 50ppm催奇形作用認めず				［ラット　混餌］ 0.08ppmで児動物に脳浮腫や水頭などの病理所見					［ラット　経口］ 11.7mg/kg以上で母動物の体重増加抑制、児動物の口蓋裂や骨格形態異常の発生頻度増加 ［ラット　経口］ 10mg/kgで母動物体重増加抑制、一腹児数減少、出生児成長抑制、児動物の膣開口遅延、脳重量低下等 ［マウス］ 胎児前肢芽培養液中への添加で発育阻害作用 催奇形性とは断定不可
がん原性	［ラット　混餌］ 154～616ppm 肝良性腫瘍		［ハムスター混餌］ 50ppm 肝、血管、甲状腺等への腫瘍	［マウス雄 混餌］ 4,8ppm 用量相関性のある肝腫瘍 ﾌﾟﾛﾓｰﾀｰ作用有	［マウス雄 混餌］ 2.5,5ppm 用量相関性のある肝腫瘍 ﾌﾟﾛﾓｰﾀｰ作用有		［マウス　混餌］ 雄2ppm,雌10ppm以上で肝腫瘍 ［ラット］ 500ppmで肝腫瘍ﾌﾟﾛﾓｰﾀｰ作用有	［マウス］ 肝腫瘍の発生増加 ［ラット］ 催腫瘍性認めず催腫瘍性の有無は結論に至らず	［マウス］ 肝腫瘍の発生増加 ［ラット］ 催腫瘍性認めず催腫瘍性の有無は結論に至らず	［ラット　混餌］ 0.5～50ppmで下垂体腺腫、副腎褐色細胞腫・上皮小体腺腫発生増加 膵腺癌の発生(頻度が低く、用量相関認めず)
生体内運命	［マウス　経口］ 100μg/day ４ヶ月で150μg程度蓄積						ヒト体内でDDEに変化して長期間残留 DDEの250ppm混餌投与で肝腫瘍	動物における排泄は遅く、動物体内に蓄積ﾁﾄｸﾛｰﾑP-450の顕著な誘導	体内で代謝されて毒性の強いﾍﾌﾟﾀｸﾛﾙ･ｴﾎﾟｷｼﾄﾞに変化 この化合物の排泄は遅く、脂肪組織等に蓄積	ﾗｯﾄ経口の吸収率20～50%。消化管吸収不良。３日後までに約70%が糞便中に排泄。腸肝循環の可能性。尿中排泄は代謝物。 肝、腎に多く分布。脂肪、脳にも分布 血漿中濃度は低い 血中半減期:14時間 脳中半減期:6.6日
変異原性								ﾌﾟﾛﾓｰﾀｰ試験(+) Ames,染色体:弱い(+)	ﾌﾟﾛﾓｰﾀｰ試験(+) 染色体：弱い(+)	Ames,染色体,小核で一部（＋）。弱い変異原性
その他	PCB混入食用油の摂取により、眼脂の増加、爪の変色、嘔吐等		ﾍｷｻｸﾛﾛﾍﾞﾝｾﾞﾝにて殺菌した種子用小麦の誤食により、晩発性皮膚ﾎﾟﾙﾌｨﾘﾝ症の発症			ｴﾝﾄﾞﾘﾝ汚染小麦粉原料のﾊﾟﾝ摂取で悪心、嘔吐、頭痛、腹部不快感、痙攣、意識喪失等 含量:48～1807ppm		ﾋﾄで嘔吐、痙攣等の急性中毒症状ｼｽｸﾛﾙﾃﾞﾝ、ﾄﾗﾝｽｸﾛﾙﾃﾞﾝ、ﾍﾌﾟﾀｸﾛﾙ、ﾉﾅｸﾛﾙ等を含む混合物	ﾍﾌﾟﾀｸﾛﾙはｸﾛﾙﾃﾞﾝの一成分。毒性ﾃﾞｰﾀもｸﾛﾙﾃﾞﾝと同様の傾向	ﾐﾄｺﾝﾄﾞﾘｱでの酸化的ﾘﾝ酸化の阻害等と推定 皮膚等に刺激作用 ﾄﾘﾌﾞﾁﾙｽｽﾞ化合物はﾋﾄ赤血球を溶血
ADI	5μg/kg/day			0.1μg/kg/day	0.1μg/kg/day	0.2μg/kg/day	5μg/kg/day	1μg/kg/day	0.5μg/kg/day	

既存の第一種特定化学物質に関する毒性評価一覧　（続）

物質名	N,N'－ｼﾞﾄﾘﾙ－p－ﾌｪﾆﾚﾝｼﾞｱﾐﾝ N－ﾄﾘﾙ－N'－ｷｼﾘﾙ－p－ﾌｪﾆﾚﾝｼﾞｱﾐﾝ N,N'－ｼﾞｷｼﾘﾙ－p－ﾌｪﾆﾚﾝｼﾞｱﾐﾝ	2,4,6-ﾄﾘ-tert-ﾌﾞﾁﾙﾌｪﾉｰﾙ	トキサフェン	マイレックス	2,2,2-トリクロロ-1,1-ビス（4-クロロフェニル）エタノール（別名ケルセン又はジコホル）	ヘキサクロロブタ-1,3-ジエン	2-（2H-1,2,3-ベンゾトリアゾール-2-イル）-4,6-ジ-tert-ブチルフェノール
指定年月日	H12.6.7	H12.8.14	H14.9.4	H14.9.4	H17.4.1	H17.4.1	H19.10.31
慢性毒性	［ラット　混餌］ 0.02%以上で （♀♂） 肝臓の絶対重量、脾臓の絶対及び相対重量並びに副腎の絶対重量の増加、副腎皮質のコレステリン様物質を含む貪食細胞増加及び血小板数の減少 （♂） アスパラギン酸アミノトランスフェラーゼ活性の上昇 （♀） 体重増加抑制、摂餌量の減少、血清中鉄濃度の低下、副腎の相対重量の増加及び脾臓の繊維化 0.1%以上で （♀♂） 血清中銅濃度、アルカリフォスファターゼ活性及びロイシンアミノペプチダーゼ活性の上昇、肝臓及び腎臓の相対重量の増加並びに肝臓の髄外造血 （♂） 血清中鉄濃度の低下、ｺﾘﾝエステラーゼ活性の上昇、トリグリセリド並びに副腎の相対重量及び腎臓の絶対重量の増加（♀） アルブミン及びリン脂質の減少、A/G比の低下 以上よりNOELは0.004%（♂：約1.8mg/kg/day,♀：約1.28mg/kg/day）と推定	［マウス］ 肝細胞の壊死、変性等、間質の線維化等の肝障害 肝硬変様の非可逆的変化の可能性	［ラット］ 2.5mg/kgで肝細胞の組織学的変化 50mg/kgで肝細胞肥大	マウス　経口］ １mg/kgで肝肥大	［ラット　混餌］ 2.2mg/kgで肝細胞肥大・副腎皮質細胞空胞化	［ラット　混餌］ 2mg/kg/day以上で、腎の組織学的変化	［ラット経口］ 0.5mg/kg雄で肝の組織学的変化（変異肝細胞等）
生殖能及び後世代に及ぼす影響	［ラット　経口］ 8mg/kgで、生存児数の減少及び胚胎児死亡率の増加		行動への影響、免疫抑制	［マウス］ 5mg/kgで同腹児数減少 1.8mg/kgで繁殖停止 ［ラット］ 25mg/kgで同腹児数減少、生存率低下	［ラット］ 2世代生殖毒性試験において250ppm(P1),25ppm(P2)で卵巣間質細胞空胞化 250ppm(F1),125ppm(F2)で新生児体重、生存率低下	［ラット］ 20あるいは7.5mg/kg/day以上で、それぞれ出生児及び新生児の体重の低下。 75mg/kg/dayで受胎率低下及び着床阻害	
催奇形性	［ラット　経口］ NOEL：（親）8mg/kg/day （児）4mg/kg/day		［マウス］ 35mg/kgで児動物に脳瘤	［ラット］ 6mg/kgで内臓異常			
がん原性	［ラット　混餌］ 慢性毒性試験２４ヶ月目に屠殺した♀において、卵巣の顆粒膜夾膜細胞腫の発生が0、0.004、0.02、0.1%の各投与群において、それぞれ２０匹中０例、１９匹中０例、１８匹中０例及び１９匹中５例に認められ、また0.1%投与群の死亡例においても１例の卵巣黄体腫が認められた		［マウス］ 肝腫瘍 ［ラット］ 甲状腺濾胞細胞癌・甲状腺腺腫（雄） 甲状腺癌（雌）	［マウス及びラット］ 肝腫瘍		［ラット］ 腎尿細管の腺腫・腺癌	
生体内運命	［ラット　混餌］ 主として糞中に排泄、代謝物の構造確認できず。 尿中への排泄は１%以下で主要な尿中排泄物はメチル基の水酸化体と思われる代謝物。 脂肪組織中濃度は血中濃度に対して♂：109～2493倍、♀：140～7972倍 肝臓中濃度は血中濃度に対して♂：7～168倍、♀：7～467倍			動物における半減期は遅く、数カ月	ラットにおける半減期は、雄で1.5～4日、雌においては4～7日。	放射標識されたHCBDを投与した場合、マウス及びラットにおける放射活性の半減期は72時間以内 腎においてHCBDの活性代謝物が蓄積し、腎毒性を示す	
変異原性			Ames陽性	優性致死試験　陰性 （ラット） Ames陰性	in vitro及び in vivo系において陰性	グルタチオン添加及び腎Ｓ9存在下でAmes陽性、SCE陽性	Ames　陰性 染色体　陰性
その他	PCB混入食用油の摂取により、眼脂の増加、爪の変色、嘔吐等				農薬事故による暴露により悪心、めまい、嘔吐等 急性毒性試験において自発運動低下、運動失調、傾眠傾向、振戦等の神経症状		
ADI	5μg/kg/day		1.25μg/kg/day	RfD: 0.2μg/kg/day	2μg/kg/day (RfD: 0.4μg/kg/day)	MRL:0.2μg/kg/day	

参考資料　３

監視化学物質への該当性の判定等に係る試験方法及び判定基準

最終改正　平成１８年７月２１日

厚生労働省医薬食品局審査管理課化学物質安全対策室
経済産業省製造産業局化学物質管理課化学物質安全室
環境省総合環境政策局環境保健部企画課化学物質審査室

化学物質の審査及び製造等の規制に関する法律に基づく化学物質の審査に係る厚生労働省、経済産業省及び環境省の関係審議会を合同で開催するに当たり、第一種監視化学物質、第二種監視化学物質及び第三種監視化学物質への該当性の判定を行うために必要とされる試験の試験成績に係る現在の判定基準等について、下記のとおりとする。

下記の基準を基本としつつ、関係審議会における専門的知見に基づく意見を踏まえ、各監視化学物質への該当性の判定を行うこととする。

記

Ｉ．試験方法

（１）新規化学物質及び既存化学物質が監視化学物質に該当するかどうかの判断は、当該新規化学物質及び既存化学物質について既に得られている知見の他、「新規化学物質に係る試験並びに第一種監視化学物質及び第二種監視化学物質に係る有害性の調査の項目等を定める省令」第２条第１項から第３項まで及び第２条の２の規定による以下の試験の試験成績に基づき行うものとされている。

①微生物等による化学物質の分解度試験（分解度試験）

②魚介類の体内における化学物質の濃縮度試験（濃縮度試験）又は１－オクタノールと水との間の分配係数測定試験（Pow 測定試験）

③ほ乳類を用いる２８日間の反復投与毒性試験（２８日間反復投与毒性試験）又はほ乳類を用いる９０日間の反復投与毒性試験（９０日間反復投与毒性試験）

④細菌を用いる復帰突然変異試験及びほ乳類培養細胞を用いる染色体異常試験又はマウスリンフォーマ TK 試験（変異原性試験）

（以下、③及び④を「スクリーニング毒性に関する試験」という。）

⑤藻類生長阻害試験、ミジンコ急性遊泳阻害試験及び魚類急性毒性試験（生態毒性試験）

（２）これらの試験は、原則として「新規化学物質等に係る試験の方法について（平成１５年１１月２１日薬食発第１１２１００２号・平成１５・１１・１３製局第２号・環保企発第０３１１２１００２号）」（以下「通知」という。）に沿って実施することとされているが、通知に定められていない試験方法（ＯＥＣＤテストガイドライン等）に基づく試験成績については、上記(1)の試験方法と同等の取扱いが可能である

と考えられ当該試験成績の信頼性が確保されていると認められる場合には、判定の際に用いることとしている。

Ⅱ．試験成績に係る判定基準

上記Ｉ．（１）に掲げる試験の試験成績に基づき判定を行う場合には、原則として以下の基準によることとしている。

（１）分解度試験

①良分解性

- ３つの試験容器のうち２つ以上でBODによる分解度が６０％以上であり、かつ３つの平均が６０％以上であること。
  - ：あわせて HPLC、GC 等の直接分析法により分解生成物が生成していないことが確認されること。
  - ：なお、通知で定められた試験方法による試験成績が上記の基準を満たさない場合であって、BOD 曲線等から試験終了後も引き続き生分解していることが示唆される場合（上昇傾向等）には、ＯＥＣＤテストガイドライン 302Ｃによる試験成績に基づいて判定を行うことができる。

②難分解性

- 良分解性でないこと。

（２）濃縮度試験又はPow 測定試験

①高濃縮性

- 濃縮倍率が5000倍以上であること。

②高濃縮性でない

以下のいずれかであること。

- 濃縮倍率が1000倍未満であること
- １－オクタノール／水分配係数（Pow）の対数が３．５未満であること。ただし、界面活性のある物質、分子量分布を有する混合物、有機金属化合物、純度の低い物質（HPLC法を除く）及び無機化合物には適用しない。

③濃縮倍率が 1000 倍以上、5000 倍未満の場合には、必要に応じ、以下の成績を考慮して高濃縮性かどうかを総合的に判断する。

- 排泄試験
- 部位別（可食部）の濃縮倍率

なお、上記の判定に当たっては、原則として、定常状態における濃縮倍率を用いることとし、定常状態での数値が得られない場合には、総合的に判断をする。また、濃縮倍率に濃度依存性が認められる場合には、必要に応じてより低濃度区での試験を行い、その成績を踏まえ判断する。

（３）スクリーニング毒性に関する試験

①細菌を用いる復帰突然変異試験

a)陽性

- いずれかの試験系で溶媒対照の２倍を超えて復帰変異誘発コロニー数が増加し、その作用に再現性又は用量依存性が認められること。
- 比活性値が概ね 1000rev/mg 以上である場合には、原則として、強い陽性と判断する。
- 陽性の場合にあって、再現性や用量依存性に乏しい場合等には、原則として、軽微な陽性と判断する。

b)陰性

- 陽性でないこと。

②ほ乳類培養細胞を用いる染色体異常試験又はマウスリンフォーマ TK 試験

a) ほ乳類培養細胞を用いる染色体異常試験

[1] 陽性

- 染色体異常を持つ細胞の出現率が陰性対照に比べ概ね１０％以上であり、その作用に再現性又は用量依存性が認められること。
- D_{20}値が 10^{-2}mg/ml 以下である場合には、原則として、強い陽性と判断する。
- 陽性の場合にあって、再現性や用量依存性に乏しい場合等、又は概ね 50%あるいはそれ以上の細胞増殖阻害が起こる濃度でのみの陽性反応等は、原則として、軽微な陽性と判断する。

[2] 陰性

- 陽性でないこと。

b) マウスリンフォーマ TK 試験

[1] 陽性

- いずれかの試験系で突然変異頻度が統計学的に有意な増加を示し、その作用に再現性又は用量依存性が認められること。
- いずれかの試験系で突然変異頻度が陰性対照の 4 倍、又は陰性対照より 400 $\times 10^{-6}$ を超えて増加している場合には、原則として、強い陽性と判断する。
- 陽性の場合にあって、再現性や用量依存性に乏しい場合、若しくは突然変異頻度が陰性対照の２倍未満である場合等、又は概ね 80%あるいはそれ以上の細胞毒性が認められる濃度でのみの陽性反応等は、原則として、軽微な陽性と判断する。

[2] 陰性

- 陽性でないこと。

③２８日間反復投与毒性試験（以下、OECD テストガイドライン４２２で定められた方法に準じて実施された試験を含む。）又は９０日間反復投与毒性試験

a)NOEL 及び発現した毒性の程度から以下の３段階に分類する。

［１］：・NOEL が概ね 25mg/kg/day 未満のもの（NOEL の推定根拠において非特異的な変化等、毒性学的に軽微な変化のみが発現した場合を除く。）

・NOEL が概ね 25mg/kg/day 以上 250mg/kg/day 未満のものであって、NOEL の推定根拠又はその他の発現した毒性において、神経行動毒性や重篤な病理組織学的な変化等、毒性学的に重要な変化（回復期の影

響については、b）Ａ又はＢに該当するものとする。）が発現したもの。

［２］：NOELが概ね250mg/kg/day未満のもの（［１］に該当するものを除く。）

［３］：NOELが概ね250mg/kg/day以上のもの。

なお、９０日間反復投与毒性試験においては、２８日間反復投与毒性試験に比べて投与期間が長いこと等を考慮しつつ、判断することとする。

b)回復試験中に見られる影響の程度から以下の３段階に分類する。なお、分類に当たっては、可逆性の程度、回復期における毒性の残存状況、遅発毒性の有無、組織学的変化に起因する生化学的な変化かどうか等を考慮する。

Ａ：回復試験期間内に回復しない病理組織学的な変化を生じさせるもの、又は遅発毒性を生じさせるもの

Ｂ：回復試験期間内に回復しない生化学的な変化を生じさせるもの

Ｃ：回復試験の期間において回復する、又は回復途上であることが示される可逆的変化

（４）生態毒性試験

藻類生長阻害試験、ミジンコ急性遊泳阻害試験及び魚類急性毒性試験の結果から以下の３段階に分類する。（藻類生長阻害試験に基づく毒性値は、原則として速度法により算出したものを用いる。以下同じ。）

［１］：３種の試験結果から得られるL(E)C50値の最小値が概ね1mg/l以下のもの。

［２］：３種の試験結果から得られるL(E)C50値のいずれかが概ね1mg/l超、10mg/l以下のもの。（［１］に該当する場合を除く。）

［３］：３種の試験結果から得られるL(E)C50値の最小値が概ね10mg/l超のもの。

（５）第一種監視化学物質の判定

既存化学物質について、（１）が難分解性であり、（２）が高濃縮性であると判断された場合であって、人及び高次捕食動物への長期毒性を有することがいずれも明らかでない場合には第一種監視化学物質として判定する。

（６）第二種監視化学物質の判定

（１）が難分解性であり、（２）が高濃縮性ではないと判断された場合であって、（３）の結果、次のいずれかに該当する場合には第二種監視化学物質として判定する。

①２８日間反復投与毒性試験又は９０日間反復投与毒性試験（以下「反復投与毒性試験等」という。）において強い毒性が示唆されるもの

（（３）③［１］に該当する場合）

②変異原性試験において強い陽性が示唆されるもの

（（３）①又は②が強い陽性の場合）

③反復投与毒性試験等において中程度の毒性を示すとともに、変異原性試験で強い陽性ではないものの陽性であるもの

（（３）③［２］に分類され、かつ、（３）①又は②が陽性（但し、軽微な陽性

である場合を除く。）の場合）

ただし、通知に規定する慢性毒性試験、生殖能及び後世代に及ぼす影響に関する試験、催奇形性試験、変異原性試験（小核試験等）、がん原性試験、生体内運命に関する試験、薬理学的試験又はこれらと試験の目的が合致している試験において、死亡、がん、長期にわたる障害、生殖能又は後世代の発生に及ぼす影響その他これらに準じて毒性学的に重要な影響が認められた知見がある場合には、必要に応じ、これらの試験成績を考慮して第二種監視化学物質に該当するか判定する。

（７）第三種監視化学物質の判定

（１)が難分解性であり、第一種特定化学物質ではないと判断された場合、以下の[１]、[２]のいずれかにより第三種監視化学物質に該当する場合には、第三種監視化学物質として判定する。

[１]（４）の結果から以下のように判定する。

①３種の試験結果から得られる L(E)C50 値の最小値が概ね 1mg/l 以下である場合（（４）[１]に該当する場合）には、第三種監視化学物質として判定する。

②３種の試験結果から得られる L(E)C50 値のいずれかが概ね 1mg/l 超、10mg/l 以下である場合（（４）[２]に該当する場合）には、以下のとおり判断する。なお、下記ａ）～ｃ）に複数該当する場合であって、第三種監視化学物質に該当するかの判定が分かれた場合においては、第三種監視化学物質として判定する。

ａ）魚類急性毒性試験の結果が該当する場合には、第三種監視化学物質として判定する。

ｂ）ミジンコ急性遊泳阻害試験の結果が該当する場合には、物質の化学構造等を考慮して個別に判断する。

c.）藻類生長阻害試験の結果が該当する場合には、以下のように判定する。

（ｉ）EC50 の値が 1mg/l 超、2mg/l 以下である場合には、第三種監視化学物質として判定する。

（ii）EC50 の値が 2mg/l 超、10mg/l 以下である場合には、第三種監視化学物質として判定しない。

③３種の試験結果から得られる L(E)C50 値の最小値が概ね 10mg/l 超である場合（（４）[３]に該当する場合）には、第三種監視化学物質とは判定しない。

[２]「第三種監視化学物質に係る有害性調査のための試験の方法について（平成１６年３月２５日平成１６・３・１９製局第６号・環保企発第０４０３２５００４号）」に定める藻類生長阻害試験、ミジンコ繁殖試験又は魚類初期生活段階毒性試験の試験結果において、少なくとも、NOEC が 0.1mg/l 以下となる場合には第三種監視化学物質として判定する。また、これらの試験以外の水生生物に対する慢性毒性を示唆する試験結果が得られた場合には、個別に判断する。

なお、上記に基づき判定が困難な物質については、類似の物質の評価及び判定の例を参考にしつつ、安全側に立脚した観点から判定する。

Ⅲ．高分子フロースキームに基づく判定

高分子フロースキームに基づき判定を行う場合には、原則として以下の基準によることとしている。

（１）以下の安定性試験の結果及び溶解性試験の結果に係る基準を満たす場合には、難分解性であり、かつ、高濃縮性ではないと判定する。

①安定性試験

・重量変化の基準
：試験前後で変化がないこと（2%以下の変化は変化とは見なさない）。

・DOC 変化の基準
：試験前後で変化がないこと（5ppm 以下の変化は変化とは見なさない）。

・ＩＲスペクトルの基準
：試験前後で変化がないこと。

・分子量変化の基準
：試験前後で変化がないこと。

②溶解性試験

a)以下の９種類の溶媒のいずれにも溶けない場合であって、特定の構造特性（架橋構造、高結晶性等）を有するか、又は酸・アルカリに不溶であること。

水、n-ｵｸﾀﾉｰﾙ、n-ﾍﾌﾟﾀﾝ、ﾄﾙｴﾝ、1,2-ｼﾞｸﾛﾛｴﾀﾝ、ｲｿﾌﾟﾛﾋﾟﾙｱﾙｺｰﾙ、ﾃﾄﾗﾋﾛﾄﾞﾌﾗﾝ(THF)、ﾒﾁﾙｲｿﾌﾞﾁﾙｹﾄﾝ(MIBK)、ｼﾞﾒﾁﾙﾎﾙﾑｱﾐﾄﾞ（DMF）

b)上記 a)以外の場合は、分子量 1000 未満の成分含有量が１%以下であること。

なお、上記①及び②の基準を満たさない場合には、分解性試験、濃縮度試験、スクリーニング毒性に関する試験、生態毒性試験の試験成績に基づき判定を行う。

（２）Ⅲ．（１）①及び②の基準を満たす場合には、以下のとおり判定を行う。

a)重金属を含まず、化学構造と長期毒性との関連性に関する知見等から判断して人への長期毒性を有することが示唆されない場合には、第二種監視化学物質に該当しないと判定する。

b) a)以外の場合には、スクリーニング毒性に関する試験の試験成績に基づき第二種監視化学物質への該当性の判定を行う。

c)以下のいずれかの場合には、第三種監視化学物質に該当しないと判定する。

（ｉ）重金属を含まず、水、酸及びアルカリに対する溶解性が確認されない場合であって、次のいずれかに該当する場合

・水への自己分散性*が確認されない場合
・水への自己分散性が確認された場合であって、カチオン性を示さない場合

＊　分散剤を含まない条件下で分散する性状を有するもの

（ii）重金属を含まず、水、酸及びアルカリに対する溶解性が確認された場合にカチオン性を示さないものであって、化学構造と動植物への毒性との関連性に関する知見等から判断して、動植物の生息又は生育に支障を及ぼすおそれを有すると示唆されない場合

d)c）以外の場合には、生態毒性試験の試験成績に基づき第三種監視化学物質への該当性の判定を行う。

「監視化学物質（指定化学物質）への該当性の判定等に係る試験方法及び判定基準」の改正履歴

制定：平成１５年４月１８日

改正：平成１６年４月３０日（指定化学物質から監視化学物質への名称変更、生態毒性試験の追加、第一種監視化学物質及び第三種監視化学物質の判定基準の追加）

改正：平成１６年６月１８日（Pow 測定試験における判定基準を 3.0 未満から 3.5 未満に変更及び Pow 測定試験における除外規定を追加）

改正：平成１７年１月１４日（高分子フロースキームに基づく第三種監視化学物質判定基準において水への自己分散性が確認された場合の基準を追加及び Pow 測定試験に HPLC 法を採用したことに伴う変更を追記）

改正：平成１７年６月２４日（マウスリンフォーマＴＫ試験、90 日間反復投与毒性試験及び慢性毒性試験等の記載を追加）

改正：平成１７年９月３０日（第三種監視化学物質において３種生物における生態毒性試験の判定基準及び水生生物に対する慢性毒性における判定基準等の記載を追記）

改正：平成１８年７月２１日（第三種監視化学物質判定基準中の藻類生長阻害試験に関し、毒性値の計算に原則として速度法を用いることを追記及び判定基準を変更）

参考資料　4

化学物質の審査及び製造等の規制に関する法律の一部を改正する法律の公布について

平成２１年５月２０日
経済産業省
厚生労働省
環境省

本日、「化学物質の審査及び製造等の規制に関する法律の一部を改正する法律」が公布されました。

１．改正の趣旨

（１）近年、安全・安心についての関心が高まる中、国民の化学物質に対する懸念も広がっている。国際的にも、すべての化学物質による人及び環境への影響を最小化することが環境サミットで合意されている。その後、欧州ではすべての化学物質を対象とした規制が平成１９年に施行されるなど、化学物質管理を巡る状況は大きく変化しつつある。

（２）化学物質の審査及び製造等の規制に関する法律（化学物質審査規制法）は、昭和４８年の制定以降に新たに流通した化学物質については厳しい事前審査を実施してきた。他方、同法制定以前から市場に存在する化学物質（既存化学物質）については、国自ら安全性評価を行い、必要に応じて同法による規制措置を講じてきたが、すべての物質を評価するには至っていない。

（３）そのため、既存化学物質の製造・輸入を行う事業者に毎年度その数量の届出を義務づけるとともに、必要に応じて有害性情報の提出を求めること等により、安全性評価を着実に実施し、我が国における厳格な化学物質管理をより一層推進する必要がある。また、今次改正によって格段に集積される情報を関係省庁間で共有し、各法令に基づく化学物質規制をより効果的なものとする。

（４）加えて、「残留性有機汚染物質に関するストックホルム条約」の規制対象に追加される物質について、国内実施法である従来の化学物質審査規制法では、条約で許容される例外的使用に対応した規定がなされていない。そのため、このような国際的な不整合を解消し、合理的な審査・規制体系を構築する。

２．改正の概要

（１）既存化学物質も含めた包括的管理制度の導入

① 既存化学物質を含むすべての化学物質について、一定数量（１トンを予定）以上の製造・輸入を行った事業者に対して、毎年度その数量等を届け出る義務を課す。

② 上記届出の内容や有害性に係る既知見等を踏まえ、優先的に安全性評価を行う必要がある化学物質を「優先評価化学物質」に指定する。（「優先評価化学物質」の新設に伴い、「第二種監視化学物質」「第三種監視化学物質」は廃止する。）

③ 必要に応じて、優先評価化学物質の製造・輸入事業者に有害性情報の提出を求めるとともに、取扱事業者にも使用用途の報告を求める。

④ 優先評価化学物質に係る情報収集及び安全性評価を段階的に進めた結果、人又は動植物への悪影響が懸念される物質については、現行法と同様に「特定化学物質」として製造・使用規制等の対象とする。

⑤ これまで規制の対象としていた「環境中で分解しにくい化学物質」に加え、「環境中で分解しやすい化学物質」についても対象とする。

（２）流通過程における適切な化学物質管理の実施

特定化学物質及び当該物質が使用された製品による環境汚染を防止するため、取扱事業者に対して、一定の取扱基準の遵守を求めるとともに、取引に際して必要な表示を行う義務を課す。

（３）国際的動向を踏まえた審査・規制体系の合理化

ストックホルム条約の規制対象となる物質について、条約で許容される例外的使用を厳格な管理の下で認めるため第一種特定化学物質に係る規制の見直しを行う等、規制の国際整合化を行う。

※ 具体的な改正点については、別紙参照。また、制度の詳細、安全性評価の方法等については、後日公表予定。

３．施行期日

本日から１年を超えない範囲において政令で定める日（平成２２年４月１日を予定）。【第１段階改正】

ただし、上記２（１）の①から④（すべての化学物質に係る製造・輸入数量等の届出、優先評価化学物質の指定、第二種・第三種監視化学物質の廃止等）については、本日から２年を超えない範囲において政令で定める日（平成２３年４月１日を予定）。【第２段階改正】

（別紙）

化学物質審査規制法の主な改正点

（引用条文は第２段階改正後のもの）

１．定義

① 難分解性の性状を有さないものを「第二種特定化学物質」として指定できるよう、自然的作用による化学的変化を生じにくいものとしている要件を削る。（第２条第３項関係）

② 「第一種監視化学物質」の名称を「監視化学物質」に改める。（第２条第４項関係）

③ その化学物質に関して得られている知見等からみて、継続的に摂取される場合に人の健康を損なうおそれがあるものでないこと等が明らかであると認められないこと等により、当該化学物質による環境の汚染により人の健康に係る被害等を生ずるおそれがあるものであるかどうかについての評価を優先的に行う必要があると認められる化学物質として厚生労働大臣、経済産業大臣及び環境大臣が指定するものを「優先評価化学物質」とする。（第２条第５項関係）

④ 既存化学物質名簿に記載されている化学物質等を「一般化学物質」とする。（第２条第７項関係）

⑤ 「第二種監視化学物質」及び「第三種監視化学物質」を廃止する。

２．新規化学物質に関する確認制度の拡大

新規化学物質の製造又は輸入開始前の届出について、高分子化合物であって、環境の汚染が生じて人の健康に係る被害等を生ずるおそれがないものとしての基準に該当する旨の厚生労働大臣、経済産業大臣及び環境大臣の確認を受けて、その新規化学物質を製造し、又は輸入するときは、当該届出を要しないこととする。（第３条第１項第６号関係）

３．一般化学物質に関する措置

一般化学物質を製造し、又は輸入した者は、一般化学物質ごとに、毎年度、前年度の製造数量又は輸入数量等を経済産業大臣に届け出なければならないこととする。（第８条関係）

４．優先評価化学物質に関する措置

① 優先評価化学物質を製造し、又は輸入した者は、優先評価化学物質ごとに、毎年度、前年

度の製造数量又は輸入数量等を経済産業大臣に届け出なければならないこととする。（第９条関係）

② 厚生労働大臣、経済産業大臣及び環境大臣は、優先評価化学物質による人の健康に係る被害等を生ずるおそれがあるものであるかどうかについての評価を行うに当たって必要があると認めるときは、その製造等の事業を営む者に対し、当該優先評価化学物質の性状に関する試験の試験成績を記載した資料の提出を求めることができることとする。（第１０条第１項関係）

③ 厚生労働大臣、経済産業大臣及び環境大臣は、優先評価化学物質の製造等の状況等からみて、その有害性に係る判定をする必要があると認めるに至ったときは、その製造等の事業を営む者に対し、有害性の調査の結果を報告すべきことを指示することができることとする。（第１０条第２項関係）

④ 業として優先評価化学物質を取り扱う者は、優先評価化学物質を他の事業者に対し譲渡し、又は提供するときは、その相手方に対し、当該優先評価化学物質の名称等の情報を提供するよう努めなければならないこととする。（第１２条関係）

５．監視化学物質に関する措置

業として監視化学物質を取り扱う者は、監視化学物質を他の事業者に対し譲渡し、又は提供するときは、その相手方に対し、当該監視化学物質の名称等の情報を提供するよう努めなければならないこととする。（第１６条関係）

６．第一種特定化学物質に関する措置

① 他の物による代替が困難であり、かつ、当該第一種特定化学物質が使用されることにより環境の汚染が生じて人の健康に係る被害等を生ずるおそれがない用途について、第一種特定化学物質の使用が制限されないこととする。（第２５条関係）

② 業として第一種特定化学物質等を取り扱う者は、第一種特定化学物質等を取り扱う場合においては、技術上の基準に従ってしなければならないこととする。（第２８条第２項関係）

③ 業として第一種特定化学物質等を取り扱う者は、第一種特定化学物質等を譲渡し、又は提供するときは、第一種特定化学物質等の容器、包装又は送り状に当該第一種特定化学物質による環境の汚染を防止するための措置等に関し表示をしなければならないこととする。（第２９条関係）

７．第二種特定化学物質に関する措置

① 環境の汚染を防止するためにとるべき措置に関する技術上の指針を遵守するべき者として、業として第二種特定化学物質等を取り扱う者を加える。（第３６条関係）

② 業として第二種特定化学物質等を取り扱う者は、第二種特定化学物質等を譲渡し、又は提供するときは、第二種特定化学物質等の容器、包装又は送り状に当該第二種特定化学物質による環境の汚染を防止するための措置等に関し表示をしなければならないこととする。（第３７条関係）

８．その他

① 優先評価化学物質、監視化学物質又は第二種特定化学物質の製造又は輸入の事業を営む者は、その製造し、又は輸入した化学物質について、その性状等に関する知見を有しているときは、当該知見等の内容を厚生労働大臣、経済産業大臣及び環境大臣に報告するよう努めなければならないこととする。（第４１条第３項関係）

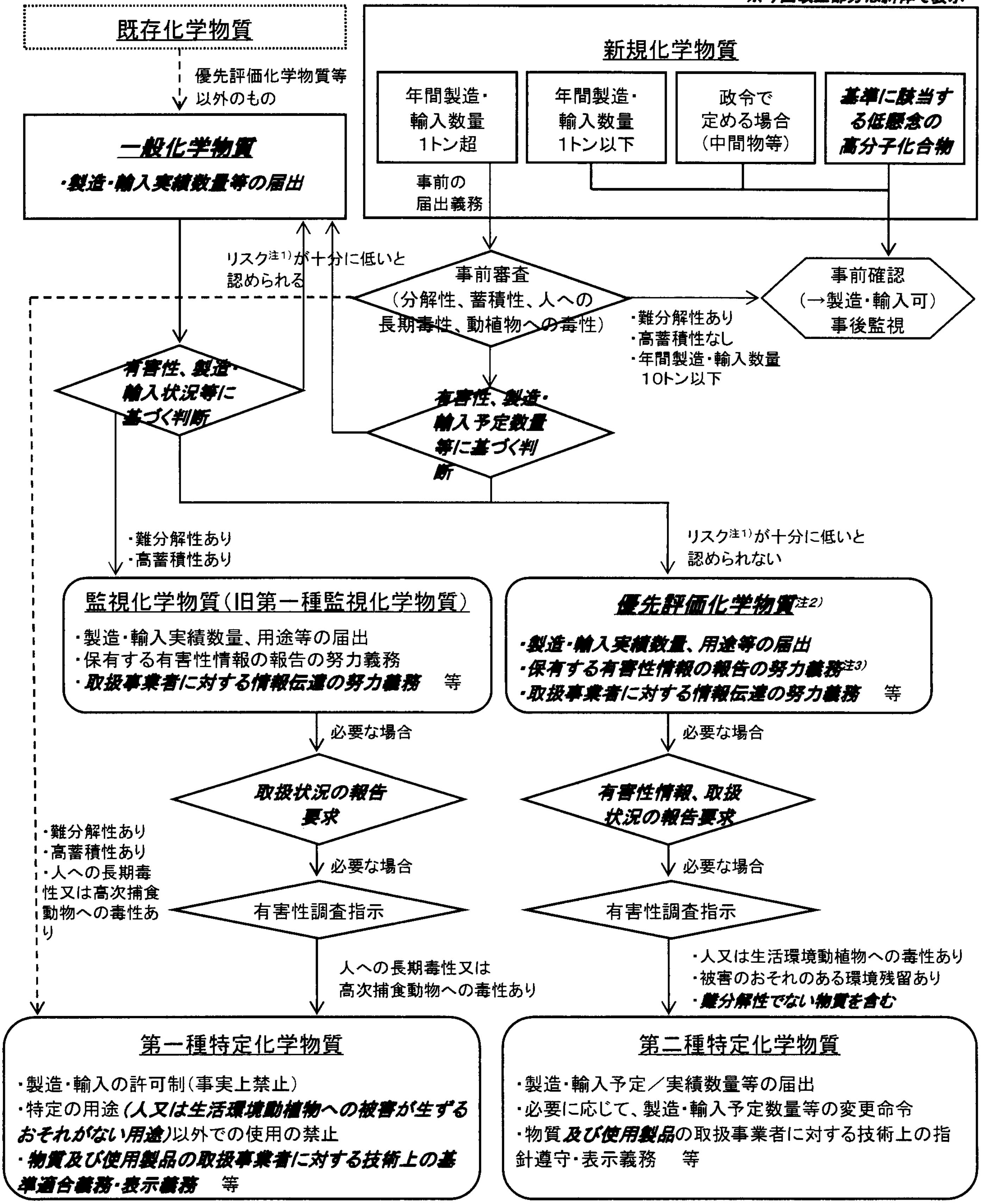
② 主務大臣は、業として優先評価化学物質を取り扱う者、業として監視化学物質を取り扱う者又は業として第二種特定化学物質等を取り扱う者に対し、その取扱いの状況について報告を求めることができることとする。（第４２条関係）

③ 厚生労働大臣、経済産業大臣又は環境大臣は、この法律に基づいて化学物質の性状等に関する知見等を得た場合において、他の法律に基づく措置に資するため、必要に応じ、当該他の法律の施行に関する事務を所掌する大臣に対し、当該知見等の内容を通知することとする。（第４７条関係）

④ 新たに定める義務について罰則を定める。（第５７～６３条関係）

（参考）改正後の化学物質審査規制法の概要

※今回改正部分は斜体で表示



注1） 本図において、リスクとは、第二種特定化学物質の要件である、「人への長期毒性又は生活環境動植物への生態毒性」及び「被害のおそれが認められる環境残留」に該当するおそれのことを指す。

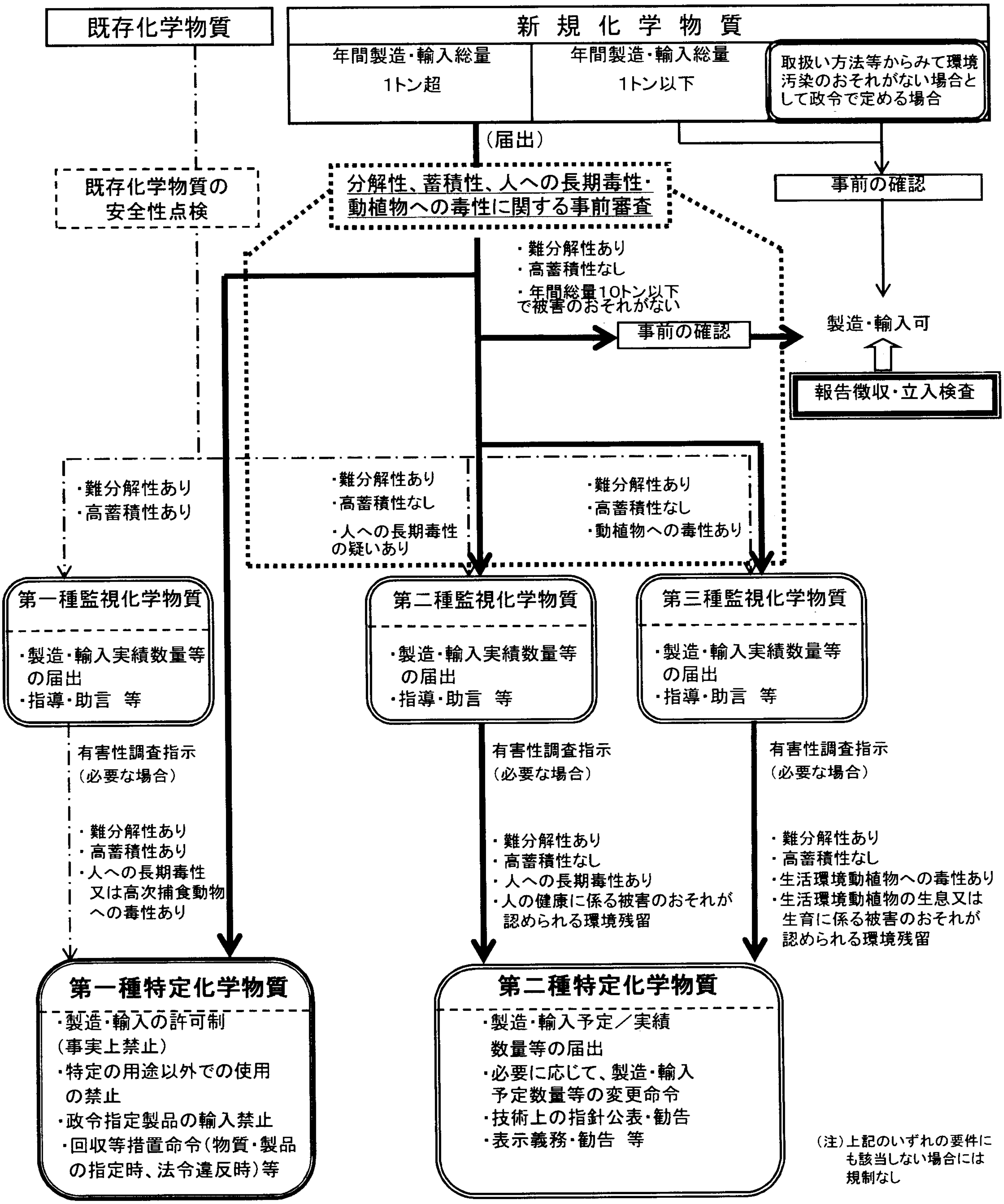
注2） 第二種及び第三種監視化学物質は廃止される。これらに指定されていた物質について、製造・輸入数量、用途等を勘案して、必要に応じて優先評価化学物質に指定される。

注3） 第二種特定化学物質にも適用される。

注4） 有害性情報を新たに得た場合の報告義務あり。（第一種特定化学物質を除く。）

注5） 必要に応じ、取扱方法に関する指導・助言あり。（第二種特定化学物質、監視化学物質、優先評価化学物質）

化学物質の審査及び製造等の規制に関する法律の制度概要



既存化学物質

既存化学物質の安全性点検

新規化学物質

年間製造・輸入総量 1トン超

年間製造・輸入総量 1トン以下

取扱い方法等からみて環境汚染のおそれがない場合として政令で定める場合

（届出）

分解性、蓄積性、人への長期毒性・動植物への毒性に関する事前審査

事前の確認

- ・難分解性あり
- ・高蓄積性なし
- ・年間総量10トン以下で被害のおそれがない

事前の確認

製造・輸入可

報告徴収・立入検査

- ・難分解性あり
- ・高蓄積性あり

- ・難分解性あり
- ・高蓄積性なし
- ・人への長期毒性の疑いあり

- ・難分解性あり
- ・高蓄積性なし
- ・動植物への毒性あり

第一種監視化学物質

- ・製造・輸入実績数量等の届出
- ・指導・助言　等

第二種監視化学物質

- ・製造・輸入実績数量等の届出
- ・指導・助言　等

第三種監視化学物質

- ・製造・輸入実績数量等の届出
- ・指導・助言　等

有害性調査指示（必要な場合）

- ・難分解性あり
- ・高蓄積性あり
- ・人への長期毒性又は高次捕食動物への毒性あり

有害性調査指示（必要な場合）

- ・難分解性あり
- ・高蓄積性なし
- ・人への長期毒性あり
- ・人の健康に係る被害のおそれが認められる環境残留

有害性調査指示（必要な場合）

- ・難分解性あり
- ・高蓄積性なし
- ・生活環境動植物への毒性あり
- ・生活環境動植物の生息又は生育に係る被害のおそれが認められる環境残留

第一種特定化学物質

- ・製造・輸入の許可制（事実上禁止）
- ・特定の用途以外での使用の禁止
- ・政令指定製品の輸入禁止
- ・回収等措置命令（物質・製品の指定時、法令違反時）等

第二種特定化学物質

- ・製造・輸入予定／実績数量等の届出
- ・必要に応じて、製造・輸入予定数量等の変更命令
- ・技術上の指針公表・勧告
- ・表示義務・勧告　等

（注）上記のいずれの要件にも該当しない場合には規制なし

○製造・輸入事業者が自ら取り扱う化学物質に関し把握した有害性情報の報告を義務付け