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Third meeting**

Geneva, 19–23 November 2007

Item 9 (a) of the provisional agenda \*

**Consideration of draft risk profiles on: commercial octabromodiphenyl ether**

**Draft risk profile: commercial octabromodiphenyl ether**

**Note by the Secretariat**

1. At its second meeting, the Persistent Organic Pollutants Review Committee adopted decision POPRC-2/6 on commercial octabromodiphenyl ether.<sup>1</sup> By paragraph 2 of the decision, the Committee decided to establish an ad hoc working group to review further the proposal to list commercial octabromodiphenyl ether in Annexes A, B, and/or C to the Convention (see documents UNEP/POPS/POPRC.2/12 and UNEP/POPS/POPRC.2/INF/4) and to develop a draft risk profile in accordance with Annex E to the Convention.
2. The members of the ad hoc working group on octabromodiphenyl ether and its observers are listed in annex V of document UNEP/POPS/POPRC.2/17.
3. A standard workplan for the preparation of a draft risk profile was adopted by the Committee at its second meeting.<sup>2</sup>
4. In accordance with decision POPRC-2/6 and the standard workplan adopted by the Committee, the ad hoc working group on octabromodiphenyl ether prepared the draft risk profile set forth in the annex to the present note. The draft risk profile has not been formally edited.

\* UNEP/POPS/POPRC.3/1/Rev.1.

<sup>1</sup> UNEP/POPS/POPRC.2/17, annex I.

<sup>2</sup> Ibid., para. 36 and annex II-A.

### **Possible action by the Committee**

5. The Committee may wish:

(a) To adopt, with any amendments which it deems appropriate, the draft risk profile set forth in the annex to the present note;

(b) To decide, in accordance with paragraph 7 of Article 8 of the Convention and on the basis of the risk profile, whether the chemical is likely as a result of its long-range transport to lead to significant adverse human health and/or environmental effects such that global action is warranted and that the proposal should proceed;

(c) To agree, depending on the decision taken under (b) above:

(i) To invite all Parties and observers to provide information pursuant to Annex F to the Convention, to establish an ad hoc working group to develop a draft risk management evaluation and to agree on a workplan for completing the draft; or

(ii) To make the risk profile available to all Parties and observers and set it aside.

**Annex**

# **COMMERCIAL OCTABROMODIPHENYL ETHER**

**DRAFT RISK PROFILE**

Draft prepared by the ad hoc working group on  
C-Octabromodiphenyl ether  
under the Persistent Organic Pollutants Review Committee  
of the Stockholm Convention

**August 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 no 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 also demonstrated for HeptaBDE, although at a lower extent 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 documented 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 is not an easy task as 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, additional concerns related to the debromination into toxic BDEs, the increasing evidence relating these chemicals with other POPs (similarities between PBDEs and PCBs; relationships with dioxins and furans), and that under Article 8, paragraph 7(a) of the Convention the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the components of c-OctaBDE, Hexa to NonaBDE, 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  $\leq 0.5\%$  Pentabromodiphenyl ether isomers,  $\leq 12\%$  Hexabromodiphenyl ether isomers,  $\leq 45\%$  Heptabromodiphenyl ether isomers,  $\leq 33\%$  OctaBDE isomers,  $\leq 10\%$  Nonabromodiphenyl ether isomers and  $\leq 0.7\%$  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)

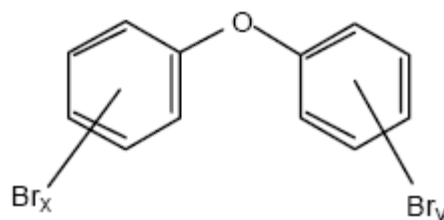
Synonyms: octabromobiphenyl oxide; octabromodiphenyl oxide; octabromo phenoxybenzene and benzene; 1,1' oxybis-, octabromo derivative

CAS Number: 32536-52-0

Molecular formula:  $C_{12}H_2Br_8O$

Molecular weight: 801.38

Chemical structure:



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  $\equiv$  polybromobiphenyl ethers – PBBEs  
 polybrominated biphenyl oxides  $\equiv$  polybromobiphenyl oxides - PBBOs  
 polybrominated diphenyl ethers  $\equiv$  polybromodiphenyl ethers - PBDPEs  
 polybrominated diphenyl oxides  $\equiv$  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 1-1 below. 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 information

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.

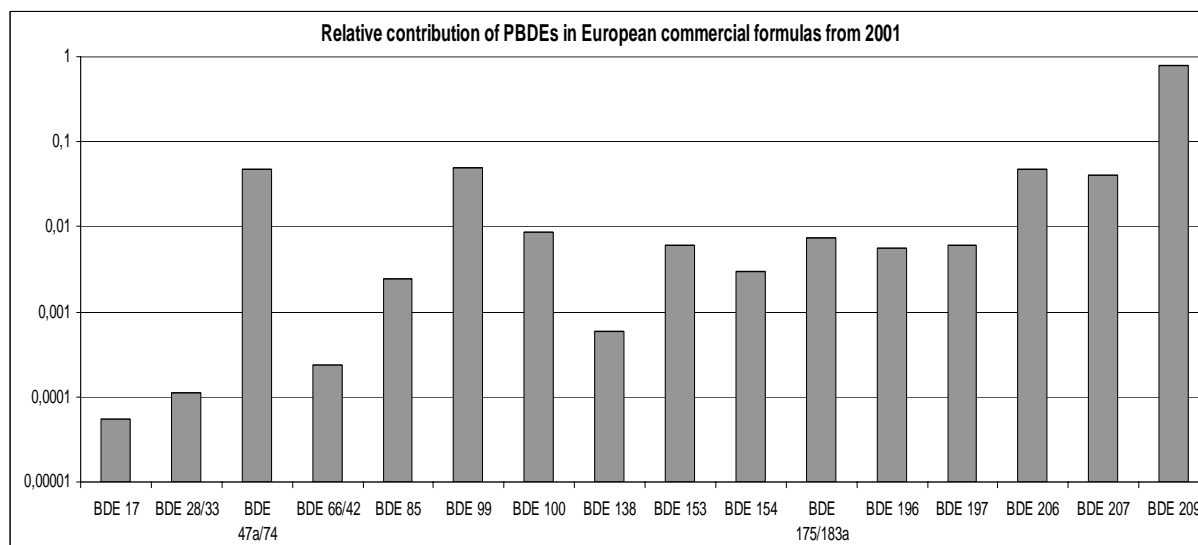
The polybrominated diphenyl ethers in general are used as flame retardants of the additive type. They are physically combined with the material being treated rather than chemically combined (as in reactive flame retardants). This means that there is the possibility that the flame retardant may diffuse 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).

Gerecke et al. (2005) reported the degradation of NonaBDE 206 and 207 and DecaBDE to OctaBDEs under anaerobic conditions using sewage sludge inoculum; 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 methanol/water 80:20 (Eriksson et al. 2001) a 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 HexaBDPE).

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 zooplankton 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  $9.1 \pm 1.1$  was observed for BDE 154, the highest concentration was found on day 15 and the depuration rate constant was  $0.032 \pm 0.016 \text{ days}^{-1}$ .

#### 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  $0.051 \pm 0.036 \text{ days}^{-1}$  and assimilation efficiencies of  $4\% \pm 3$  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 ( $t_{1/2}$ 's) for some BDE congeners (e.g., BDE-85 and -190) were much lower than expected based on their Kow, whereas  $t_{1/2}$ '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  $0.016 \text{ days}^{-1}$  in juvenile American kestrels (*Falco sparverius*), with a retention of about 50% of the administered dose.

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 extent 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 documented 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.

### 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 the environment and 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, it is very unlikely to assume a long range transport only for DecaBDE and not also 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/m<sup>3</sup>.

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/m<sup>2</sup>/year (Moon et al., 2007a). In northwest China, the measurements of total PBDEs (8.3 ± 4.0 pg/m<sup>3</sup>) 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/m<sup>3</sup>) and along the coastal line of Java, Indonesia (values of 15 pg/m<sup>3</sup>). 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 µg/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 0.1 µg/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.

### 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 were 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).

### 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  $\Sigma$ 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 ( $\Sigma$ PBDE) were – at an average of 7.17 ng  $\Sigma$ PBDE g (lipid)<sup>-1</sup> – 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 industrial 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  $\mu$ g/kg ww for each isomer and maximum values above 10  $\mu$ g/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.

The assessment for Octa and NonaBDE is more uncertain. They have been detected in biota but not in remote areas. However, the relatively low contribution of these congeners in commercial mixtures (Figure 1 indicates that the contribution of Nona and Octa are one and two orders of magnitude lower than DecaBDE), and the limited potential for

bioaccumulation due to metabolism (which could be related to demobromination) may require lower limits of detection for a proper assessment than those used in previous studies.

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 an 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.

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 available information focuses on less than ten congeners and some mixtures, from theoretically 80 different possible congeners.

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 extent 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 is not an easy task as 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 and 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, additional concerns related to the debromination into toxic BDEs, the increasing evidence relating these chemicals with other POPs (similarities between PBDEs and PCBs; relationships with dioxins and furans), and that under Article 8, paragraph 7(a) of the Convention the lack of full scientific certainty shall not prevent a proposal from proceeding, it is concluded that the components of c-OctaBDE, Hexa to NonaBDE, 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.
- Brevik 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. Occurrence 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.

- Eriksson J, Jakobsson E, Marsh G, Bergman Å, 2001. Photo decomposition of brominated diphenyl ethers in methanol/water. Abstracts. The Second International Workshop on Brominated Flame Retardants. BFR 2001 Stockholm. May 14-16. Stockholm University, Sweden. p. 203-206.
- 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, Alae 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 of four seabird 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, Alae 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, Alae 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, Hågberg 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. Occurrence 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.
- 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, Ikonoumou 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, Llompert 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 the common carp (*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, Braekveit 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
-