

Polybrominated Diphenyl Ethers (PBDEs)
[Tetra-, Penta-, Hexa-, Hepta-, Octa-, Nona- and Deca-
Congeners]

[CAS Nos. 40088-47-9, 32534-81-9, 36483-60-0, 68928-80-3,
32536-52-0, 63936-56-1, 1163-19-5]

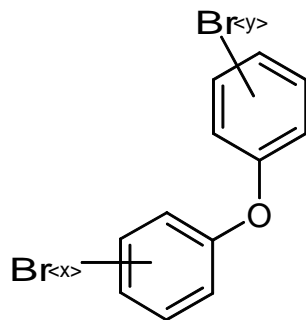


Figure 1: Base structure of PBDEs considered in this assessment, where $x + y = 4-10$

Introduction

The *Canadian Environmental Protection Act, 1999* (CEPA 1999) requires the federal Ministers of Health and the Environment to conduct screening assessments for substances that have been categorized to determine whether they pose a risk to human health or the environment. On the basis of a screening assessment, the Ministers can propose to take no further action in respect of the substance, to add the substance to the Priority Substances List for a more in-depth assessment or to recommend that the substance be added to the List of Toxic Substances in Schedule 1 of the Act.

Screening assessments of risks to human health address responsibilities of the Minister of Health under Paragraph 64(c) of CEPA 1999 to determine whether or not a substance is “entering or may enter the environment in a quantity or concentration or under conditions that constitute or may constitute a danger in Canada to human life or health.” Screening health assessments focus in a preliminary fashion on conservative effect levels for critical endpoints and upper-bounding estimates of exposure, after consideration of all relevant identified information. Decisions based on the nature of the critical effects and margins between conservative effect levels and estimates of exposure take into account confidence in the completeness of the identified databases on both exposure and effects, within a screening context. Additional background information on screening health assessments conducted under this program is available at <http://www.hc-sc.gc.ca/exsd-dse>.

Several polybrominated diphenyl ethers (PBDEs) have been identified as meeting the Section 73 criteria for persistence and/or bioaccumulation and inherent toxicity to non-human organisms and nominated for inclusion in a pilot phase for preparation of screening assessments under CEPA 1999.

This screening assessment report on human health aspects and associated unpublished supporting working documentation were prepared by evaluators within the Existing Substances Division of Health Canada, and their content was reviewed at several meetings of senior Divisional staff. The documents were subsequently externally reviewed for adequacy of data coverage and defensibility of the conclusions. The assessment reports on health and environmental aspects were approved by the joint Environment Canada/Health Canada CEPA Management Committee. The supporting working documentation is available upon request by e-mail from ExSD@hc-sc.gc.ca. Information on the screening environmental assessment is available at <<http://www.ec.gc.ca/substances/ese>>.

Information identified as of July 2003 was considered for inclusion in this screening health assessment.¹ The critical information and considerations upon which the assessment is based are summarized below.

Identity, Uses and Sources of Exposure

PBDEs are a class of substances that contain an identical base structure (see Figure 1), but differ in the number of attached bromine atoms (n = 1–10). Of the 10 congener groups (comprising 209 individual congeners in total), seven are on the Domestic Substances List (i.e., n=4-10) and are considered in this assessment (Table 1).

Table 1: List of PBDEs considered in the assessment

Congener group	Acronym	CAS No.	No. of individual congeners
Tetrabromodiphenyl ether	TeBDE	40088-47-9	42
Pentabromodiphenyl ether	PeBDE	32534-81-9	46
Hexabromodiphenyl ether	HxBDE	36483-60-0	42
Heptabromodiphenyl ether	HeBDE	68928-80-3	24
Octabromodiphenyl ether	OcBDE	32536-52-0	12
Nonabromodiphenyl ether	NoBDE	63936-56-1	3
Decabromodiphenyl ether	DeBDE	1163-19-5	1

PBDEs do not occur naturally in the environment; they are generally produced synthetically as mixtures, referred to as commercial pentabromodiphenyl ether (ComPeBDE, which is predominantly a mixture of TeBDE, PeBDE and HxBDE), commercial octabromodiphenyl ether (ComOcBDE, which contains mainly HeBDE, OcBDE and HxBDE,

¹ The potential impact of preliminary results of a monitoring study conducted by Health Canada (2003) was also considered.

but may also contain small amounts of PeBDE, NoBDE and DeBDE) and commercial decabromodiphenyl ether (ComDeBDE, of which current formulations are almost entirely DeBDE, with a small amount of NoBDE) (IPCS, 1994). The identical base structure and combination of congener groups within the different commercial mixtures support consideration of a category approach to assessment of these compounds. In addition, to the extent that the data permit comparison, consideration of these compounds as a group is supported by trends in physical/chemical properties with increasing degree of bromination.

Results of a Section 71 survey under CEPA 1999 (Environment Canada, 2001) indicate that uses of PBDEs in Canada are similar to those in other countries, primarily as additive flame retardants in a wide variety of consumer products, such as internal electric/electronic components of and casings for household appliances/electronics (e.g., hair dryers, televisions, computers), furniture upholstery and cushioning, and wire and cable insulation (IPCS, 1994). Commercial DeBDE is primarily used in the high-impact polystyrene component of electronic equipment housings and is also the only commercial PBDE product used to flame retard upholstery textiles. Commercial OcBDE is predominantly used in acrylonitrile butadiene styrene to flame retard business equipment housings. Commercial PeBDE is used almost exclusively in flexible polyurethane foam, which is used as cushioning in upholstered furniture (Wenning, 2002).

Hazard Characterization and Exposure Assessment

The majority of identified data relevant to the evaluation of risk to human health relate to the commercial mixtures, with much less information being available for individual congeners. Based on preliminary assessment of the available toxicological data, the critical effects and effect levels for the ComPeBDE, ComOcBDE and ComDeBDE commercial mixtures, as well as each of the congener groups considered in this assessment (where possible), are presented in Table 2, with a more extensive summary of the health effects associated with each presented in Table 3. It appears that the critical effects of PBDEs occur on the liver and neurobehavioural development. Due to the limited nature of the database for some substances, confidence in the assessment for each PBDE congener group and commercial mixture varies.

In consideration of the above information, the critical effect level considered most appropriate for assessment of risk to human health in a screening context is the conservative value of 0.8 mg/kg-bw (for PeBDE), based on neurobehavioural effects consisting of changes in locomotion, rearing and total activity in a dose- and time-related manner observed in neonatal mice administered a single oral dose by gavage on postnatal day 10 and observed for a subsequent 5-month period (Eriksson et al., 1998, 2001). Effects on neurobehavioural development have also been observed in neonatal mice exposed to higher doses of PeBDE on different postnatal days (Eriksson et al., 1999, 2002; Viberg et al., 2000 [abstract], 2002b), as well as in pups exposed to PeBDE via maternal administration (although there was no relationship between dose and magnitude of effect) (Branchi et al., 2002, 2003). However, no effect on motor activity was observed in rats exposed to up to 100 mg ComPeBDE/kg-bw per

day from gestation day 6 to postnatal day 21 (Taylor et al., 2002 [abstract], 2003 [abstract]; MacPhail et al., 2003 [abstract]), although effects similar to those observed at 0.8 mg PeBDE/kg-bw were observed by the same group of investigators in neonatal mice administered single, relatively low doses of TeBDE, HxBDE and DeBDE (Eriksson et al., 1998, 2001; Viberg et al., 2001a [abstract], 2001b [abstract], 2002a [abstract], 2003; Viberg, 2002 [personal communication]). Since these congener groups are also present in the commercial mixtures ComPeBDE, ComOcBDE and ComDeBDE, it is appropriate to consider this Lowest-Observed-Effect Level (LOEL) for PeBDE as critical in a screening assessment of the health hazard of this group of PBDEs as a whole. [N.B.: Although a lower LOEL of 0.44 mg/kg-bw per day was observed for ComPeBDE, this LOEL was based on alterations in hepatic enzyme activities, and no histopathological changes in the liver were observed at this or higher doses (Carlson, 1980b).] In addition, critical LOELs for other effects (changes in liver weight or histopathology) observed in longer-term studies in rodents administered ComPeBDE or ComOcBDE are within an order of magnitude of this conservative LOEL. This conservative critical effect level is also considered protective for the small increases in the incidence of liver tumours observed in mice and rats chronically administered much higher doses of DeBDE, in view of the lack of weight of evidence for the genotoxicity of the PBDEs.

Available data upon which to base estimates of population exposure to PBDEs are quite disparate, in that some authors reported concentrations in media for individual congeners or congener groups, whereas others reported levels of total PBDEs, without further identification of specific congeners measured. Thus, it is difficult to derive meaningful estimates of exposure to individual congeners or congener groups. For the purpose of this screening assessment, in light of the similarity of health effects associated with the various PBDEs considered here, critical effect levels were compared with an upper-bounding estimate of exposure to total PBDEs (i.e., the tetra- to deca- derivatives considered here), as a basis for development of conservative margins for the purposes of screening.

Based on reported concentrations of PBDEs in ambient and indoor air,² water, various foodstuffs, human breast milk and dust, along with standard reference values for six different age groups, including breast-fed infants, an upper-bounding estimate of daily intake of total PBDEs (i.e., the tetra- to deca- derivatives considered here) ranges from 0.2 to 2.6 µg/kg-bw per day for various age groups of the general population in Canada. Food (including breast milk) represents the principal source of exposure for the majority of the age groups (although dust was the principal source of exposure for the 0- to 6-month-old non-breast-fed age group) (see Table 4). The age group with potentially the greatest exposure was 0- to 6-month-old breast-fed infants, with breast milk accounting for 92% of the exposure. Consistent with the limited intent of screening assessments to develop upper-bounding estimates of exposure, this estimate was based

² In a recent study by Health Canada (2003), for which only preliminary results are available, the maximum concentration of PBDEs (TeBDE to HeBDE) in samples of residential indoor air from 72 homes in Ottawa was 3.6 ng/m³. However, this value does not impact upon the upper-bounding estimates of daily intake of total PBDEs because of the relatively small contribution of air to overall exposure.

on the maximum concentration of PBDEs measured in breast milk (589 ng/g lipid). It should be noted, though, that the mean and median values in the study were approximately 40- and 200-fold less, respectively, than this value (i.e., 15 and 2.9 ng/g lipid, respectively) (Ryan and Patry, 2001a, 2001b; Ryan et al., 2002a, 2002b). The authors noted that there was much interindividual variation in levels of PBDEs in breast milk, with some very high values for individual samples. Based on limited data, levels of PBDEs in human breast milk in Canada appear to be increasing with time (e.g., there was a 9-fold increase in mean concentration between 1992 and 2001) (Ryan et al., 2002a).

These upper-bounding estimates of exposure are considered conservative, in that they are based on summed estimates for all congeners for which data are available. Data for each of the congeners were based on the highest measured concentrations for many media. Upper-bounding estimates of intake in food for subpopulations consuming more traditional or country foods, based on limited information on maximum concentrations of PBDEs and consumption patterns of such foods, are not substantially greater (i.e., less than 2-fold). Emissions of PBDEs from consumer products that have been treated with flame retardant formulations containing these substances (e.g., televisions or computer casings) could contribute to overall exposure. However, intakes via inhalation from such sources estimated on the basis of information on average use patterns and concentrations in emissions are negligible (i.e., up to 5×10^{-4} µg/kg-bw per day) in comparison with intake from food. Similarly, estimates of intake from dermal contact with dust or oral contact with household products treated with flame retardants containing the penta- and octa- derivatives (ENVIRON International Corporation, 2003a, 2003b) are also negligible in comparison with intake from food.

In view of the nature of the effects determined to be critical (i.e., neurodevelopmental effects in mice following neonatal exposure), consideration of the upper-bounding estimate of intake in breast-fed infants as the critical measure of exposure in this screening assessment is considered appropriate. Alternative approaches to developing upper-bounding estimates of exposure were also considered (e.g., back-calculation of intakes based on first-order kinetic modelling of limited data on levels in the blood of the general population, and comparison of estimated body burden for the critical study in experimental animals with that estimated for breast-fed infants). However, confidence in the resulting estimates, which result in margins of exposure approximately 10-fold less than that presented below, is extremely low, owing to the considerable limitations of the relevant data on biological half-lives of PBDEs in humans and their seeming inconsistency with what would be expected based on relevant physical/chemical properties (i.e., the high log octanol/water partition coefficient of PBDEs).

Proposed Conclusion for Human Health

Comparison of the critical effect level (i.e., 0.8 mg/kg-bw) with the upper-bounding deterministic estimate of exposure (i.e., the metric of exposure in which confidence is greatest) for the intake of total PBDEs for the potentially most highly exposed age group (2.6 µg/kg-bw per day in breast-fed infants) results in a margin of exposure of approximately 300. As discussed

above, the selected critical effect level and deterministic estimates of exposure are considered quite conservative, consistent with the preliminary nature of screening health assessments.

The conservative nature of the margin of exposure does not, however, take into account the potential continuing increase in body burden of PBDEs (based on data for breast milk), should similar use patterns continue. Prediction of trends in body burdens is precluded by the limited information on the toxicokinetics of PBDEs in humans and animals and transfer from human breast milk to infants as well as the uncertainty in half-lives for removal processes for PBDEs in environmental media. Determination of the adequacy of this margin to address elements of uncertainty associated with limitations of the database for health effects and population exposure (in which confidence overall is considered to be moderate), intraspecies and interspecies variations in sensitivity as well as the biological adversity or severity of the effects deemed critical requires additional in-depth evaluation of the relevant data. It also requires development of additional, more meaningful information on population exposure to PBDEs.

However, in view of the proposed recommendation to add PBDEs to the List of Toxic Substances based on environmental considerations (<http://www.ec.gc.ca/substances/ese/>), more in-depth evaluation of PBDEs from a human health perspective is considered a low priority, unless information becomes available to indicate that measures recommended to control exposure of environmental organisms to PBDEs will not be protective for human health. This priority is based on the smaller margin between the most conservative estimated critical values for exposure and effects on the environment (<http://www.ec.gc.ca/substances/ese/>) in comparison with that for human health (approximately 7^3 versus 300) and experience in other countries that risk management actions to protect the environment have resulted in a reduction of exposure of humans.

Proposed Recommendation to the Ministers of the Environment and Health

On the basis principally of environmental considerations, it is proposed that these PBDEs as a group be considered “toxic” as defined in Section 64 of CEPA 1999 (see <http://www.ec.gc.ca/substances/ese/>).

³ Based on comparison of the values which formed the basis for the risk quotient analysis for wildlife (i.e., a LOEL of 2 mg/kg bw/day of ComPeBDE for effects on the liver in rats (Great Lakes Chemical Corporation, 1984) and the dose ingested by mink consuming fish containing 1.25 mg/kg ww total PBDEs (Johnson and Olson, 2001)).

Table 2: Overview of critical health effects and effect levels for PBDE congener groups and commercial products

	LOEL (mg/kg-bw per day)	Endpoint	Reference
TeBDE	10.5	Developmental behavioural (mouse)	Eriksson et al., 2001
PeBDE	0.8	Developmental behavioural (mouse)	Eriksson et al., 1998, 2001
HxBDE	0.9	Developmental behavioural (mouse)	Viberg et al., 2002a (abstract)
HeBDE	–	–	
OcBDE	–	–	
NoBDE	–	–	
ComPeBDE	2	Liver histopathology: subchronic dietary study (rat)	Great Lakes Chemical Corporation, undated a
ComOcBDE	5	Liver weight: subchronic dietary study (rat)	Great Lakes Chemical Corporation, 1987
ComDeBDE/DeBDE	2.22	Developmental behavioural (mouse)	Viberg et al., 2001a (abstract), 2001b (abstract), 2003; Viberg, 2002 (personal communication)

Table 3: Summary of health effects information for PBDE congener groups and commercial mixtures¹

Endpoint	Congener group					Commercial mixture			
	TeBDE	PeBDE	HxBDE	HeBDE	O c B D E	N o B D E	ComPeBDE	ComOcBDE	ComDeBDE/DeBDE
Acute toxicity: oral				Lowest oral LD₅₀ (rabbit) = >2000 mg/kg-bw (Kopp, 1990)			Lowest oral LD₅₀ (rat) = 5000 mg/kg-bw (Pharmakon Research International Inc., 1984) [Additional studies: Great Lakes Chemical Corporation, undated a / 1982 / 1988 / Dow Chemical Company, 1977 / Ameribrom Inc., 1990; Fowles et al., 1994]	Lowest oral LD₅₀ (rat) = >5000 mg/kg-bw (Kopp, 1990) [Additional studies: Great Lakes Chemical Corporation, 1982 / 1987 / 1988 / 1990; Kalk, 1982]	Lowest oral LD₅₀ (rat) = >2000 mg/kg-bw [77.4% DeBDE, 21.8% NoBDE, 0.8% OcBDE] (Norris et al., 1973 / 1974 / 1975a / 1975c) [Additional studies: Great Lakes Chemical Corporation, undated b / 1982 / 1984; Kitchin et al., 1992 / 1993 / Kitchin and Brown, 1994]
Acute toxicity: inhalation							Lowest inhalation LC₅₀ (rat) = >200 000 mg/m ³ (Great Lakes Chemical Corporation, undated a) [Additional studies: / Dow Chemical Company, 1977 / Great Lakes Chemical Corporation, 1982 / 1988 / Kopp, 1990; Haskell Laboratory, 1987]	Lowest inhalation LC₅₀ (rat) = >50 000 mg/m ³ (U.S. EPA, 1986) [Additional studies: Great Lakes Chemical Corporation, 1987 / 1988]	Lowest inhalation LC₅₀ (rat) = >48 200 mg/m ³ (Great Lakes Chemical Corporation, undated b) [Additional studies: / Great Lakes Chemical Corporation, 1982; 1984]
Acute toxicity: dermal							Lowest dermal LD₅₀ (rabbit) = >2000 mg/kg-bw (Great Lakes Chemical Corporation, undated a) [Additional studies: / Dow Chemical Company, 1977 / Great Lakes Chemical Corporation, 1982 / 1988]	Lowest dermal LD₅₀ (rat) = >2000 mg/kg-bw (Great Lakes Chemical Corporation, 1987) [Additional studies: / Great Lakes Chemical Corporation, 1982 / 1990]	Lowest dermal LD₅₀ (rabbit) = >2000 mg/kg-bw (Great Lakes Chemical Corporation, undated b) [Additional studies: / Great Lakes Chemical Corporation, 1982; 1984]

Endpoint	Congener group					Commercial mixture			
	TeBDE	PeBDE	HxBDE	HeBDE	O c B D E	N o B D E	ComPeBDE	ComOcBDE	ComDeBDE/DeBDE
Short-term repeated-dose toxicity	<p>Lowest oral (gavage) LOEL (rat and mouse) = 18 mg/kg-bw per day: decreased thyroxine levels (2,2',4,4'-TeBDE, 98% purity, 14 days)</p> <p>(Hallgren and Darnerud, 1998 / 2002; Darnerud and Thuvander, 1998)</p> <p>[Additional studies: / Thuvander and Darnerud, 1999 / Hallgren et al., 2001]</p>						<p>Lowest oral (diet) LOEL (rat) = 5 mg/kg-bw per day: increased absolute and relative liver weights (28 days)</p> <p>(Great Lakes Chemical Corporation, undated a)</p> <p>[Additional studies: / Dow Chemical Company, 1977 / Great Lakes Chemical Corporation, 1982 / 1988; Carlson, 1980a; Von Meyerinck et al., 1990; Fowles et al., 1994; Darnerud and Thuvander, 1998 / Thuvander and Darnerud, 1999 / Hallgren et al., 2001; Zhou et al., 2001]</p>	<p>Lowest oral (diet) LOEL (rat) = 5 mg/kg-bw per day: increased absolute and relative liver weights (28 days)</p> <p>(Great Lakes Chemical Corporation, 1987)</p> <p>[Additional studies: / Great Lakes Chemical Corporation, 1988; Dow Chemical Company, 1982 / Ethyl Corporation, 1990; Carlson, 1980a; Zhou et al., 2001]</p> <p>Lowest inhalation LOEC (rat) = 12 mg/m³: dose-related hepatic lesions (14 days)</p> <p>(Great Lakes Chemical Corporation, 1987)</p> <p>[Additional study: / Great Lakes Chemical Corporation, 1988]</p>	<p>Lowest oral (diet) LOEL (rat) = 80 mg/kg-bw per day: enlarged livers, generative cytoplasmic changes in the kidney and thyroid hyperplasia (77.4% DeBDE, 21.8% NoBDE, 0.8% OcBDE, 30 days)</p> <p>(Sparschu et al., 1971 / Norris et al., 1973 / 1974 / 1975a / Kociba et al., 1975a)</p> <p>[Additional studies: Great Lakes Chemical Corporation, undated b / 1982 / 1984; Carlson, 1980a; NTP, 1986; Zhou et al., 2001]</p>

Endpoint	Congener group					Commercial mixture			
	TeBDE	PeBDE	HxBDE	HeBDE	O c B D E	N o B D E	ComPeBDE	ComOcBDE	ComDeBDE/DeBDE
Subchronic toxicity							<p>Lowest oral (diet) LOEL (rat) = 2 mg/kg-bw per day: liver cell degeneration and necrosis (composition not stated, 90 days)</p> <p>(Great Lakes Chemical Corporation, undated a)</p> <p>[Additional studies: / Dow Chemical Company, 1977 / Great Lakes Chemical Corporation, 1982 / 1988 / Wil Research Laboratories Inc., 1984; Carlson, 1980b]</p>	<p>Lowest oral (diet) LOEL (rat) = 5 mg/kg-bw per day (100 ppm): increased absolute and relative liver weights (composition not stated, 13 weeks)</p> <p>(Great Lakes Chemical Corporation, 1987)</p> <p>[Additional studies: / International Research and Development Corporation, 1977 / Great Lakes Chemical Corporation, 1988; Carlson, 1980b]</p> <p>Lowest inhalation LOEC (rat) = 15 mg/m³: centrilobular hepatocellular hypertrophy (13 weeks)</p> <p>(Great Lakes Chemical Corporation, 2001)</p>	<p>No effects observed in mice at highest dose of 8060 mg/kg-bw per day (99% DeBDE, 13 weeks)</p> <p>(NTP, 1986)</p> <p>[Additional study: Hazleton Laboratories, 1979a; 1979b; Rutter and Machotka, 1979]</p>
Carcinogenicity/ chronic toxicity								<p>Increased incidence of neoplastic nodules in the liver (adenomas) in rats at ≥ 1120 mg/kg-bw per day (diet); no increase in incidence of hepatic carcinomas (103 weeks)</p> <p>Increased incidence of hepatocellular adenomas and carcinomas combined in mice at ≥ 3200 mg/kg-bw per day (diet, 103 weeks)</p> <p>(NTP, 1986 / Huff et al., 1989)</p>	

Endpoint	Congener group					Commercial mixture			
	TeBDE	PeBDE	HxBDE	HeBDE	O c B D E	N o B D E	ComPeBDE	ComOcBDE	ComDeBDE/DeBDE
									<p>Lowest oral (diet) non-neoplastic LOEL (rat) = 2240 mg/kg-bw per day: thrombosis, degeneration of the liver, fibrosis of the spleen and lymphoid hyperplasia</p> <p>(NTP, 1986 / Huff et al., 1989)</p> <p>[Additional studies: Kociba et al., 1975a / 1975b / Norris et al., 1975a / 1975b / Dow Chemical Company, 1994]</p>
Genotoxicity and related endpoints: <i>in vivo</i>									<p>Negative: rat bone marrow (cytogenetic aberrations), rat hepatic (DNA damage measured by alkaline elution)</p> <p>(Norris et al., 1975c; Kitchin et al., 1992 / 1993 / Kitchin and Brown, 1994)</p>

Endpoint	Congener group					Commercial mixture			
	TeBDE	PeBDE	HxBDE	HeBDE	O c B D E	N o B D E	ComPeBDE	ComOcBDE	ComDeBDE/DeBDE
Genotoxicity and related endpoints: <i>in vitro</i>	<p>Positive: mammalian cells (intragenic recombination)</p> <p>(Helleday et al., 1999)</p>						<p>Negative: <i>S. typhimurium</i>, <i>S. cerevisiae</i> (mutagenicity)</p> <p>(Great Lakes Chemical Corporation, undated a)</p> <p>[Additional studies: Dow Chemical Company, 1977 / Great Lakes Chemical Corporation, 1982 / 1988 / Ethyl Corporation, 1985 / Ameribrom Inc., 1990; Chemische Fabrik Kalk GmbH, 1978; Dead Sea Bromide Works, 1984; Zeiger et al., 1987]</p> <p>Positive: <i>S. typhimurium</i></p> <p>(ISC Chemicals Ltd., 1977)</p> <p>Weak positive: human peripheral blood lymphocytes (chromosomal aberrations) (no composition data provided)</p> <p>(Microbiological Associates Inc., 1996a / 1996b)</p>	<p>Negative: <i>S. typhimurium</i>, <i>S. cerevisiae</i> (mutagenicity), human fibroblast cells (DNA damage), Chinese hamster ovary cells (sister chromatid exchange), human peripheral blood lymphocytes (chromosome aberrations)</p> <p>(Great Lakes Chemical Corporation, 1982 / 1987 / 1988; Microbiological Associates Inc., 1996c / 1996d; Great Lakes Chemical Corporation, 1999)</p>	<p>Negative: <i>S. typhimurium</i>, <i>S. cerevisiae</i> (mutagenicity), <i>E. coli</i> WP2 <i>uvrA</i> (mutagenicity), Syrian hamster embryo (cell transformation), mouse lymphoma (mutagenicity), Chinese hamster ovary cells (sister chromatid exchange and chromosomal aberrations)</p> <p>(Shoichet and Ehrlich, 1977; Great Lakes Chemical Corporation, undated b / 1984 / 1988; 1982; NTP, 1986; McGregor et al., 1988 / Myrh et al., 1990 / Henry et al., 1998; LeBoeuf et al., 1996; MA Bioservices Inc., 1998)</p> <p>Indeterminant: BALB-C-3T3 cells (transformation)</p> <p>(Matthews et al., 1993)</p>

Endpoint	Congener group					Commercial mixture			
	TeBDE	PeBDE	HxBDE	HeBDE	O c B D E	N o B D E	ComPeBDE	ComOcBDE	ComDeBDE/DeBDE
Neurodevelopmental toxicity	<p>Lowest oral (gavage) LOEL (mouse) = 10.5 mg/kg-bw: change in activity patterns and habituation capability (2,2',4,4'-TeBDE >98%, one dose on postnatal day 10)</p> <p>(Eriksson et al., 2001)</p>	<p>Lowest oral (gavage) LOEL (mouse) = 0.8 mg/kg-bw: change in activity patterns and habituation (2,2',4,4',5-PeBDE >98%, one dose on postnatal day 10)</p> <p>(Eriksson et al., 1998, 2001)</p> <p>[Additional studies: Viberg et al., 2000 (abstract) / 2002b / Eriksson et al., 1999 / 2002; Branchi et al., 2002, 2003]</p>	<p>Lowest oral LOEL (mouse) = 0.9 mg/kg-bw: impaired spontaneous motor behaviour, learning and memory (2,2',4,4',5,5'-HxBDE, no purity data, one dose on postnatal day 10)</p> <p>(Viberg et al., 2002a [abstract])</p>				<p>Lowest oral (gavage) LOEL (rat) = <100 mg/kg-bw per day (not further specified): decreased cue-based performance in fear conditioning test (no composition data, gestation day 6 to postnatal day 21); no change in motor activity observed up to 100 mg/kg-bw per day</p> <p>(Taylor et al., 2003 [abstract])</p> <p>[Additional studies: Gilbert and Crofton, 2002 (abstract); Taylor et al., 2002 (abstract); MacPhail et al., 2003 (abstract)]</p>		<p>Lowest oral (gavage) LOEL (mouse) = 2.22 mg/kg-bw: changes in spontaneous behaviour (one dose on postnatal day 3)</p> <p>(Viberg et al., 2001a [abstract] / 2001b [abstract] / 2003 / Viberg, 2002 [personal communication])</p>

Endpoint	Congener group					Commercial mixture			
	TeBDE	PeBDE	HxBDE	HeBDE	O c B D E	N o B D E	ComPeBDE	ComOcBDE	ComDeBDE/DeBDE
Developmental/ reproductive toxicity (see also Neurodevel- opmental toxicity)							Lowest oral (gavage) LOEL (rat) = 3 mg/kg-bw per day: decreased thyroxine (product DE-71, no composition data, postnatal days 23–53) (Stoker et al., 2003 [abstract]) [Additional studies: Argus Research Laboratories Inc., 1985b / BFRIP, 1990 / Hoberman et al., 1998 (abstract); Zhou et al., 2000 (abstract) / 2002; Taylor et al., 2002 (abstract); 2003 (abstract); Laws et al., 2003 (abstract)]	Lowest oral (gavage) LOEL (rabbit) = 15 mg/kg-bw per day: increased liver weight (0.2% PeBDE, 8.6% HxBDE, 45% HeBDE, 33.5% OcBDE, 11.2% NoBDE, 1.4% DeBDE, gestation days 7–19) (Breslin et al., 1989) [Additional studies: U.S. EPA, 1986 (determined same as Argus Research Laboratories Inc., 1985a, which states purity to be 6.9% HxBDE, 46.8% HeBDE, 35.9% OcBDE, 10.4% NoBDE) / Hoberman et al., 1998 (abstract); Great Lakes Chemical Corporation, 1987 / 1988] Lowest inhalation LOEC (rat) = 200 mg/m ³ : lack of corpora lutea (no composition data, 13-week study) (Great Lakes Chemical Corporation, 2001)	Lowest oral (gavage) LOEL (rat) = 1000 mg/kg-bw per day: increased early resorptions (composition: 97% DeBDE, 2.66% NoBDE) (Hardy et al., 2002) [Additional studies: Norris et al., 1973 / 1974 / 1975a / 1975c / Schwetz et al., 1975; Hanley, 1985 / U.S. EPA, 1989]

Notes:

- No-Observed-Effect Levels (NOELs) were reported only when no LOELs were available.
- ComDeBDE and DeBDE were not separated due to the lack of reporting of purity and the high purity of the current commercial product.
- Lower effect levels identified that did not indicate a dose–response relationship, statistical significance and/or toxicological relevance were not included in the summary table.
- / used between studies suspected to be the same study.
- ; used between studies suspected to be different studies.

Table 4: Upper-bounding estimate of PBDE daily intake for the general population

Route of exposure	Estimated intake ($\mu\text{g}/\text{kg}\cdot\text{bw}$ per day) of PBDEs by various age groups							
	0–6 months ¹			0.5–4 years ⁴	5–11 years ⁵	12–19 years ⁶	20–59 years ⁷	60+ years ⁸
	formula fed ²	breast fed ³	not formula fed					
Ambient air ⁹	7.7×10^{-5}	7.7×10^{-5}	7.7×10^{-5}	1.7×10^{-4}	1.3×10^{-4}	7.3×10^{-5}	6.3×10^{-5}	5.5×10^{-5}
Indoor air ¹⁰	4.4×10^{-4}	4.4×10^{-4}	4.4×10^{-4}	9.3×10^{-4}	7.3×10^{-4}	4.1×10^{-4}	3.6×10^{-4}	3.1×10^{-4}
Drinking water ¹¹	1.4×10^{-3}	2.4	5.2×10^{-7}	5.9×10^{-7}	4.6×10^{-7}	2.6×10^{-7}	2.8×10^{-7}	2.9×10^{-7}
Food ¹²			2.0×10^{-2}	5.8×10^{-1}	4.8×10^{-1}	2.7×10^{-1}	2.6×10^{-1}	1.7×10^{-1}
Soil/dust ¹³	2.3×10^{-1}	2.3×10^{-1}	2.3×10^{-1}	3.6×10^{-1}	1.2×10^{-1}	2.8×10^{-2}	2.4×10^{-2}	2.3×10^{-2}
Total intake	2.3×10^{-1}	2.6	2.5×10^{-1}	9.5×10^{-1}	6.0×10^{-1}	3.0×10^{-1}	2.8×10^{-1}	1.9×10^{-1}

¹ Assumed to weigh 7.5 kg, to breathe 2.1 m³ of air per day and to drink 0.2 L/day (not formula fed) and to ingest 30 mg of soil per day. Consumption of food groups reported in EHD (1998).

² Formula-fed infants are assumed to have an intake rate of 0.75 kg of formula per day. TeBDE to HeBDE congeners were identified in a composite sample of baby formula at a value of 14 ng/kg (Ryan, undated [unpublished data]). This study was the only data point for the medium.

³ The sum of the maximum concentrations of TeBDE to HeBDE identified in 72 samples of human breast milk collected in 1992 in Canada was 589 ng/g fat (Ryan and Patry, 2001a, 2001b; Ryan et al., 2002a, 2002b). Breast-fed children 0–6 months of age are assumed to have an intake rate of 0.75 kg of breast milk per day (EHD, 1998). The percent fat of human breast milk has been estimated at 4% (U.S. EPA, 1997). No data on levels of OcBDE, NoBDE or DeBDE in human milk were identified. Data considered in the selection of critical data also included Darnerud et al. (1998, 2002), Meironyte et al. (1998), Ryan and Patry (2000), Strandman et al. (2000), Atuma et al. (2001), Papke et al. (2001), Hori et al. (2002), Meironyte Guvenius et al. (2002) and Ohta et al. (2002).

⁴ Assumed to weigh 15.5 kg, to breathe 9.3 m³ of air per day, to drink 0.7 L of water per day and to ingest 100 mg of soil per day. Consumption of food groups reported in EHD (1998).

⁵ Assumed to weigh 31.0 kg, to breathe 14.5 m³ of air per day, to drink 1.1 L of water per day and to ingest 65 mg of soil per day. Consumption of food groups reported in EHD (1998).

⁶ Assumed to weigh 59.4 kg, to breathe 15.8 m³ of air per day, to drink 1.2 L of water per day and to ingest 30 mg of soil per day. Consumption of food groups reported in EHD (1998).

- ⁷ Assumed to weigh 70.9 kg, to breathe 16.2 m³ of air per day, to drink 1.5 L of water per day and to ingest 30 mg of soil per day. Consumption of food groups reported in EHD (1998).
- ⁸ Assumed to weigh 72.0 kg, to breathe 14.3 m³ of air per day, to drink 1.6 L of water per day and to ingest 30 mg of soil per day. Consumption of food groups reported in EHD (1998).
- ⁹ The maximum sum of the PBDEs (not all congeners were specified, but the majority of the value was from TeBDE to HxBDE congener groups) was 2.2 ng/m³, measured in 14 ambient air samples from the Yukon in the year 1994–1995 (Bidleman et al., 2001). Canadians are assumed to spend 3 hours outdoors each day (EHD, 1998). Data considered in the selection of critical data also included Bergman et al. (1999), Dodder et al. (2000), Alae et al. (2001), Sjodin et al. (2001), Strandberg et al. (2001), Gouin et al. (2002) and Harner et al. (2002).
- ¹⁰ No data on levels of PBDEs in residential indoor air were identified. Three samples of indoor air from “domestic” sources in the United Kingdom were analysed, and the sum of one congener of TeBDE, two congeners of PeBDE and two congeners of HxBDE was reported at a maximum value of 1.6 ng/m³ (Wijesekera et al., 2002). Six samples of indoor air from a laboratory in Norway were analysed, and one HeBDE congener was not detected (detection limit = 0.006 ng/m³) (Thomsen et al., 2001). Two samples of air from a teaching hall in Sweden were analysed, and DeBDE was reported at a maximum concentration of 0.17 ng/m³ (Sjodin et al., 2001). No data were available for OcBDE or NoBDE. These values were added together and used to calculate the upper-bounding estimate of exposure. Canadians are assumed to spend 21 hours indoors each day (EHD, 1998). Data considered in the selection of critical data also included Bergman et al. (1999) and Pettersson et al. (2001).
- ¹¹ No data on levels of PBDEs in drinking water were identified. As a surrogate, the maximum value of PBDEs as a group (13 pg/L) detected in surface water from Lake Ontario was used (Luckey et al., 2001 [abstract]). Data considered in the selection of critical data also included Environment Agency Japan (1983, 1989, 1991).
- ¹² The concentrations of the sum of PBDEs were reported in 49 specific food items; the highest food item values were assumed to represent the concentration in each of the eight food groups (dairy, fats, vegetables, cereal products, meat and poultry, eggs, mixed dishes and fish) that include these food items. A concentration of zero was assumed for the remaining four food groups (fruits; foods primarily sugar; nuts and seeds; and soft drinks, alcohol, coffee, tea). Values for the TeBDE to HeBDE congeners were reported in a Canadian study of 40 food composite samples. The maximum values used in the upper-bounding estimate of exposure were for fat (113 ng/kg), cheese (62 ng/kg), meat (1183 ng/kg), egg (332 ng/kg), mixed dishes (207 ng/kg), cereal products (70 ng/kg) and vegetables (104 ng/kg) (Ryan, undated [unpublished data]). Twenty-one samples of salmon from Lake Michigan collected in 1996 identified a maximum of 148.6 ng/g wet weight for TeBDE to HxBDE (Manchester-Neesvig et al., 2001). HeBDE was detected in marine fish (0.030 ng/g whole weight) sampled in the Yukon (Ryan, undated [unpublished data]). No data on levels of OcBDE in food were identified. One study in the United Kingdom used the commercial OcBDE product DE-79 for identification and found levels of up to 12 µg/kg wet weight in fish muscle (Allchin et al., 1999). Neither DeBDE nor NoBDE was detected in farmed or wild salmon from British Columbia, with a detection limit of 0.65 pg/g and 1.04 pg/g wet weight, respectively (Easton et al., 2002). Samples of chicken fat from the southern United States contained a maximum of 0.01 ng OcBDE/g (unspecified isomer), 0.04 ng NoBDE/g (unspecified isomer) and 2.91 ng DeBDE/g (Huwe et al., 2002). The maximum values or detection limits were added together and used to estimate the upper-bounding estimate of exposure. Data considered in the selection of critical data also included Kruger (1988), DeBoer (1990), Jansson et al. (1993), Sellstrom et al. (1993, 1998), Longanathan et al. (1995), Haglund et al. (1997), Alae et al. (1999, 2002), Asplund et al. (1999a, 1999b), Ikonomou et al. (1999, 2002), Olsson et al. (1999), Dodder et al. (2000, 2002), Hale et al. (2000, 2001), Christensen and Platz (2001), Johnson and Olson (2001), Jones et al. (2001), Moisey et al. (2001), Zegers et al. (2001), Boon et al. (2002), Christensen et al. (2002), Jacobs et al. (2002), Luross et al. (2002), Norstrom et al. (2002), Ohta et al. (2002), Rice et al. (2002), Wakeford et al. (2002), Wijesekera et al. (2002) and Rayne et al. (2003).
- ¹³ No data on levels of TeBDE to HeBDE in soil not influenced by point sources were identified. As a surrogate, the sum of the maxima of one congener of TeBDE (BDE47) and two congeners of PeBDE (BDE99, 100) was reported as 35 760 ng/g in household dust from Massachusetts (Rudel et al., 2003). The sum of the maximum

values of a further congener of TeBDE (BDE49), PeBDE (BDE85), HxBDE (BDE153, 154), HeBDE (BDE183) and DeBDE was reported as 20 443 ng/g in household dust from Germany (Knoth et al., 2002). No data on levels of OcBDE in soil or dust were available. OcBDE was detected in sediment from Japan at a maximum level of 22 µg/kg dry weight (Environment Agency Japan, 1989, 1991). These values were added together and used as a surrogate for soil in the upper-bounding estimate of exposure. Data considered in the selection of critical data also included Sellstrom et al. (1998), Allchin et al. (1999), Christensen and Platz (2001), DeBoer et al. (2000), DeBoer and Allchin (2001), Hale et al. (2001, 2002), Leonards et al. (2001), Pettersson et al. (2001), Dodder et al. (2002), Matscheko et al. (2002) and Rayne et al. (2003).

References

- Alaee, M., Luross, J., Sergeant, D.B., Muir, D.C.G., Whittle, D.M. and Solomon, K. 1999. Distribution of polybrominated diphenyl ethers in the Canadian environment. *Organohalogen Compd.* 40: 347–350.
- Alaee, M., Cannon, C., Muir, D., Blanchard, P., Brice, K. and Fellin, P. 2001. Spatial distribution and seasonal variation of PBDEs in Arctic and Great Lakes air. *Organohalogen Compd.* 52: 26–29.
- Alaee, M., Luross, J.M., Whittle, D.M. and Sergeant, D.B. 2002. Bioaccumulation of polybrominated diphenyl ethers in the Lake Ontario pelagic food web (abstract). Unpublished report from the 4th Annual Workshop on Brominated Flame Retardants in the Environment, June 17–18, Burlington, Ontario.
- Allchin, C.R., Law, R.J. and Morris, S. 1999. Polybrominated diphenylethers in sediments and biota downstream of potential sources in the UK. *Environ. Pollut.* 105: 197–207.
- Ameribrom Inc. 1990. Letter to U.S. Environmental Protection Agency regarding 8D submission for pentabromodiphenyl ether with attachments (NTIS/OTS0526014; Document No. 86-900000434).
- Argus Research Laboratories Inc. 1985a. Embryo/fetal toxicity and teratogenic potential study of Saytex 111 administered orally via gavage to pregnant rats (final report — draft), with cover letter dated 05/07/85 (NTIS/OTS0509725).
- Argus Research Laboratories Inc. 1985b. Initial submission: embryo/fetal toxicity and teratogenic potential study of Saytex 115 administered orally via gavage to crl:cobs cd (SD) br presumed pregnant rats (NTIS/OTS0000973; Document No. FYI-OTS-0794-0973).
- Asplund, L., Hornung, M., Peterson, R.E., Turesson, K. and Bergman, A. 1999a. Levels of polybrominated diphenyl ethers (PBDEs) in fish from the Great Lakes and Baltic Sea. *Organohalogen Compd.* 40: 351–354.
- Asplund, L., Athanasiadou, M., Sjodin, A., Bergman, A. and Borjeson, H. 1999b. Organohalogen substances in muscle, egg and blood from healthy Baltic salmon (*Salmo salar*) and Baltic salmon that produced offspring with the M74 syndrome. *Ambio* 28(91): 67–76.
- Atuma, S., Aune, M., Darnerud, P.O., Cnattingius, S., Wernroth, M.L. and Wicklund-Glynn, A. 2001. Polybrominated diphenyl ethers (PBDEs) in human milk from Sweden. *In*: R.L. Lipnick, B. Jansson, D. Mackay and M. Petreas (eds.), *Persistent bioaccumulative toxic chemicals. II. Assessment and new chemicals*. American Chemical Society, Washington, D.C. (ACS Symposium Series 773).

Bergman, A., Athanasiadou, M., Wehler, E.K. and Sjodin, A. 1999. Polybrominated environmental pollutants: Human and wildlife exposures. *Organohalogen Compd.* 43: 89–92.

BFRIP (Brominated Flame Retardant Industry Panel). 1990. Brominated flame retardants. A review of recent research (compiled by BFRIP and the European Brominated Flame Retardant Industry Panel). BFRIP, West Lafayette, Indiana (unpublished report No. III/4143/90, submitted to the World Health Organization by BFRIP) [cited in IPCS, 1994].

Bidleman, T.F., Alaei, M. and Stern, G. 2001. New persistent toxic chemicals in the environment. *In*: S. Kalhok (ed.), *Synopsis of research conducted under the 2000/2001 Northern Contaminants Program*. Department of Indian and Northern Affairs, Ottawa. pp. 93–104.

Boon, J.P., Lewis, W.E., Tjoen-a-choy, M.R., Allchin, C.R., Law, R.J., DeBoer, J., Ten Hallers-Tjabbes, C.C. and Zegers, B.N. 2002. Levels of polybrominated diphenyl ether (PBDE) flame retardants in animals representing different trophic levels of the North Sea food web. *Environ. Sci. Technol.* 36: 4025–4032.

Branchi, I., Alleva, E. and Costa, L.G. 2002. Effects of perinatal exposure to a polybrominated diphenyl ether (PBDE99) on mouse neurobehavioural development. *Neurotoxicology* 23: 375–384.

Branchi, I., Capone, F., Alleva, E. and Costa, L.G. 2003. Polybrominated diphenyl ethers: neurobehavioral effects following developmental exposure. *Neurotoxicology* 24: 449–462.

Breslin, W.J., Kirk, H.D. and Zimmer, M.A. 1989. Teratogenic evaluation of a polybromodiphenyl oxide mixture in New Zealand White rabbits following oral exposure. *Fundam. Appl. Toxicol.* 12: 151–157.

Carlson, G.P. 1980a. Induction of xenobiotic metabolism in rats by short-term administration of brominated diphenylethers. *Toxicol. Lett.* 5: 19–25 [cited in IPCS, 1994].

Carlson, G.P. 1980b. Induction of xenobiotic metabolism in rats by brominated diphenylethers administered for 90 days. *Toxicol. Lett.* 6: 207–212 [cited in IPCS, 1994].

Chemische Fabrik Kalk GmbH. 1978. Ames metabolic activation test to assess the potential mutagenic effect of Bromkal 70-5 DE. Unpublished report, Huntington Research Centre (Report No. 86-900000400) [cited in European Communities, 2000].

Christensen, J.H. and Platz, J. 2001. Screening of polybrominated diphenyl ethers in blue mussels, marine and freshwater sediments in Denmark. *J. Environ. Monit.* 3: 543–547.

- 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(6): 631–638.
- Darnerud, P.O. and Thuvander, A. 1998. Studies on immunological effects of polybrominated diphenyl ether (PBDE) and polychlorinated biphenyl (PCB) exposure in rats and mice. *Organohalogen Compd.* 35: 415–418.
- Darnerud, P.O., Atuma, S., Aune, M., Cnattingius, S., Wernroth, M.L. and Wicklund-Glynn, A. 1998. Polybrominated diphenyl ethers (PBDEs) in breast milk from primiparous women in Uppsala county, Sweden. *Organohalogen Compd.* 35: 411–414.
- 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.
- Dead Sea Bromide Works. 1984. Penta-bromo-diphenyl-ether: Assessment of it's [sic] mutagenic potential in histidine auxotrophs of *Salmonella typhimurium*. Unpublished report, Life Sciences Research Ltd. (Report No. 84/DSB006/064) [cited in European Communities, 2000].
- DeBoer, J. 1990. Brominated diphenyl ethers in Dutch freshwater and marine fish. *Organohalogen Compd.* 2: 315–318.
- DeBoer, J. and Allchin, C. 2001. An indication of temporal trends in environmental PBDE levels in Europe. *Organohalogen Compd.* 52: 13–17.
- DeBoer, J., Van der Horst, A. and Wester, P.G. 2000. PBDEs and PBBs in suspended particulate matter, sediments, sewage treatment plant in- and effluents and biota from the Netherlands. *Organohalogen Compd.* 47: 85–88.
- Dodder, N.G., Strandberg, B. and Hites, R.A. 2000. Concentrations and spatial variations of polybrominated diphenyl ethers in fish and air from the northeastern United States. *Organohalogen Compd.* 47: 69–72.
- Dodder, N.G., Strandberg, B. and Hites, R.A. 2002. Concentrations and spatial variations of polybrominated diphenyl ethers and several organochlorine compounds in fishes from the northeastern United States. *Environ. Sci. Technol.* 36(2): 146–151.
- Dow Chemical Company. 1977. Initial submission: summaries of acute toxicity studies with pentabromodiphenyl oxide in rats, with cover letter dated 06/23/92 (NTIS/OTS0540414; Document No. 88-920004066).

Dow Chemical Company. 1982. Mixed lower brominated diphenyl oxides: results of a 4-week dietary feeding and 18 week recovery study in Sprague-Dawley rats, with cover letter dated 03/08/90 (NTIS/OTS0522263; Document No. 86-900000193).

Dow Chemical Company. 1994. Initial submission: results of a two-year dietary feeding study with decabromodiphenyl oxide (DBDPO) in rats (NTIS/OTS0001103; Document No. FYI-OTS-0794-1103).

Easton, M.D.L., Luszniak, D. and Von der Geest, E. 2002. Preliminary examination of contaminant loadings in farmed salmon, wild salmon and commercial salmon feed. *Chemosphere* 46: 1053–1074.

EHD (Environmental Health Directorate). 1998. Exposure factors for assessing total daily intake of priority substances by the general population of Canada. Unpublished report. December 1998. Priority Substances Section, Environmental Health Directorate, Health Canada, Ottawa.

ENVIRON International Corporation. 2003a. Voluntary Children's Chemical Evaluation Program Pilot (VCCEPP) Tier 1 assessment of the potential health risks to children associated with exposure to the commercial octabromodiphenyl ether products CAS No. 32536-52-0. Prepared for Great Lakes Chemical Corporation.

ENVIRON International Corporation. 2003b. Voluntary Children's Chemical Evaluation Program Pilot (VCCEPP) Tier 1 assessment of the potential health risks to children associated with exposure to the commercial pentabromodiphenyl ether products CAS No. 32534-81-9. Prepared for Great Lakes Chemical Corporation.

Environment Agency Japan. 1983. Environmental monitoring of chemicals. Environmental survey report of F.Y. 1980 and 1981. Office of Health Studies, Department of Environmental Health, Tokyo [cited in IPCS, 1994].

Environment Agency Japan. 1989. Chemicals in the environment. Report on environmental survey and wildlife monitoring of chemicals in F.Y. 1986 and 1987. Office of Health Studies, Department of Environmental Health, Tokyo [cited in IPCS, 1994].

Environment Agency Japan. 1991. Chemicals in the environment. Report on environmental survey and wildlife monitoring of chemicals in F.Y. 1988 and 1989. Office of Health Studies, Department of Environmental Health, Tokyo [cited in IPCS, 1994].

Environment Canada. 2001. *Canadian Environmental Protection Act, 1999*. Notice with respect to certain substances on the Domestic Substances List (DSL). *Canada Gazette* 135(46): 4194–4211 (<http://canadagazette.gc.ca/partI/2001/20011117/pdf/g1-13546.pdf>).

- Eriksson, P., Jakobsson, E. and Fredriksson, A. 1998. Developmental neurotoxicity of brominated flame-retardants, polybrominated diphenyl ethers and tetrabromo-bis-phenol A. *Organohalogen Compd.* 35: 375–377.
- Eriksson, P., Viberg, H., Jakobsson, E., Orn, U. and Fredriksson, A. 1999. PBDE 2,2',4,4',5-pentabromodiphenyl ether causes permanent neurotoxic effects during a defined period of neonatal brain development. *Organohalogen Compd.* 40: 333–336.
- Eriksson, P., Jakobsson, E. and Fredriksson, A. 2001. Brominated flame retardants: a novel class of developmental neurotoxicants in our environment. *Environ. Health Perspect.* 109: 903–908.
- Eriksson, P., Viberg, H., Jakobsson, E., Orn, U. and Fredriksson, A. 2002. A brominated flame retardant 2,2',4,4',5-pentabromodiphenyl ether: uptake, retention and induction of neurobehavioral alterations in mice during a critical phase of neonatal brain development. *Toxicol. Sci.* 67: 98–103.
- Ethyl Corporation. 1985. Initial submission: genetic toxicology *Salmonella*/microsomal assay of Saytex 115 (pentabromodiphenyloxide) (NTIS/OTS0000974; Document No. FYI-OTS-0794-0974).
- Ethyl Corporation. 1990. Letter to U.S. Environmental Protection Agency concerning the list of submitted studies on octabromodiphenyl ether, with attachments (NTIS/OTS0522188; Document No. 86-900000117).
- European Communities. 2000. European Union risk assessment report — Diphenyl ether, pentabromo deriv. European Chemicals Bureau, Existing Substances, 1st Priority List, Vol. 5.
- European Communities. 2003. European Union risk assessment report — Diphenyl ether, octabromo deriv. European Chemicals Bureau, Existing Substances, 1st Priority List, Vol. 6.
- Fowles, J.F., Fairbrother, A.F., Baecher-Steppan, L. and Kerkvliet, N.I. 1994. Immunological and endocrine effects of the flame-retardant pentabromodiphenyl ether (DE-71) in C57BL/6J mice. *Toxicology* 86: 49–61.
- Gilbert, M.E. and Crofton, K.M. 2002. Developmental exposure to polybrominated diphenyl ethers does not alter synaptic transmission or LTP in hippocampus. *Toxicologist* 66(1–S): 132 (abstract).
- Gouin, T., Thomas, G.O., Cousins, I., Barber, J., Mackay, D. and Jones, K.C. 2002. Air–surface exchange of polybrominated diphenyl ethers and polychlorinated biphenyls. *Environ. Sci. Technol.* 36(7): 1426–1434. Supporting information available at <http://pubs.acs.org/subscribe/journals/esthag/suppinfo/36/i07/es011105k/es011105k_s.pdf>.

Great Lakes Chemical Corporation. Undated a. Toxicity data of pentabromodiphenyloxide. West Lafayette, Indiana (unpublished report submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Great Lakes Chemical Corporation. Undated b. Toxicity data of decabromodiphenyloxide. West Lafayette, Indiana (unpublished report submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Great Lakes Chemical Corporation. 1982. Product and data information on decabromodiphenyl oxide, octabromodiphenyl oxide and pentabromodiphenyl oxide, with attachments (NTIS/OTS0525626; Document No. 44-8227036).

Great Lakes Chemical Corporation. 1984. Initial submission: letter to U.S. Environmental Protection Agency re: tetrabromobisphenol A, pentabromoethylbenzene, decabromodiphenyl ether and dibromopropyl acrylate, with attachments, dated 01/11/84 (NTIS/OTS0001105; Document No. FYI-OTS-0794-1105).

Great Lakes Chemical Corporation. 1987. Toxicity data of octabromo-diphenyloxide (DE-79). West Lafayette, Indiana (unpublished data submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Great Lakes Chemical Corporation. 1988. Initial submission: letter to U.S. Environmental Protection Agency regarding ITC request for information on brominated flame retardants (53 FR5466), with attachments, dated 05/17/88 (NTIS/OTS0001106; Document No. FYI-OTS-0794-1106).

Great Lakes Chemical Corporation. 1990. Great Lakes DE-79tm: Product information. West Lafayette, Indiana (report submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Great Lakes Chemical Corporation. 1999. Toxicity data on OBDPO. *In vitro* mammalian chromosome aberration test. Final report. Unpublished laboratory report, BioReliance [cited in European Communities, 2003].

Great Lakes Chemical Corporation. 2001. Initial submission: letter to U.S. Environmental Protection Agency summarizing 90-day inhalation toxicity study of oxide in albino rats, dated 05/25/01 (NTIS/OTS0574171; Document No. 88010000148).

Haglund, P.S., Zook, D.R., Buser, H.R. and Hu, J. 1997. Identification and quantification of polybrominated diphenyl ethers and methoxy-polybrominated diphenyl ethers in Baltic biota. *Environ. Sci. Technol.* 31: 3281–3287.

- Hale, R.C., La Guardia, M.J., Harvey, E.P., Mainor, T.M., Duff, W.H., Gaylor, M.O., Jacobs, E.M. and Mears, G.L. 2000. Comparison of brominated diphenyl ether fire retardant and organochlorine burdens in fish from Virginia Rivers (USA). *Organohalogen Compd.* 467: 65–68.
- Hale, R.C., La Guardia, M.J., Harvey, E.P., Mainor, T.M., Duff, W.H. and Gaylor, M.O. 2001. Polybrominated diphenyl ether flame retardants in Virginia freshwater fishes (USA). *Environ. Sci. Technol.* 35(23): 4585–4591.
- Hale, R.C., La Guardia, M.J., Harvey, E. and Mainor, T.M. 2002. Potential role of fire retardant-treated polyurethane foam as a source of brominated diphenyl ethers to the US environment. *Chemosphere* 46: 729–735.
- Hallgren, S. and Darnerud, P.O. 1998. Effects of polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs) and chlorinated paraffins (CPs) on thyroid hormone levels and enzyme activities in rats. *Organohalogen Compd.* 35: 391–394.
- Hallgren, S. and Darnerud, P.O. 2002. Polybrominated diphenyl ethers (PBDEs), polychlorinated biphenyls (PCBs) and chlorinated paraffins (CPs) in rats — testing interactions and mechanisms for thyroid hormone effects. *Toxicology* 177: 227–243.
- Hallgren, S., Sinjari, T., Hakansson, H. and Darnerud, P.O. 2001. Effects of polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) on thyroid hormone and vitamin A levels in rats and mice. *Arch. Toxicol.* 75: 200–208.
- Hanley, T.R., Jr. 1985. Decabromodiphenyl oxide: A summary of an oral teratology study in Sprague-Dawley rats. Dow Chemical Company, Midland, Michigan (unpublished report submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel [cited in IPCS, 1994]).
- Hardy, M.L., Schroeder, R., Biesemeier, J. and Manor, O. 2002. Prenatal oral (gavage) developmental toxicity study of decabromodiphenyl oxide in rats. *Int. J. Toxicol.* 21: 83–91.
- Harner, T., Ikonou, M., Shoeib, M., Stern, G. and Diamond, M. 2002. Passive air sampling results for polybrominated diphenyl ethers along an urban–rural transect. Unpublished report from the 4th Annual Workshop on Brominated Flame Retardants in the Environment, June 17–18, Burlington, Ontario.
- Haskell Laboratory. 1987. Initial submission: Process, safety & handling, and toxicity info on mono-, di-, and trimethylamine; pentabromochlorocyclohexane; tetrabromodichlorocyclohexane; tribromodichlorocyclohexane* (NTIS/OTS0000943; Document No. FYI-OTS-0794-0943).

Hazleton Laboratories. 1979a. Initial submission: 13-week subchronic feeding study in rats with decabromodiphenyl oxide (NTIS/OTS0001093; Document No. FYI-OTS-0794-1093).

Hazleton Laboratories. 1979b. Initial submission: final report: 13-week sub-chronic feeding study in mice with decabromodiphenyl oxide (NTIS/OTS0001102; Document No. FYI-OTS-0794-1102).

Health Canada. 2003. Personal communication (e-mail message from J. Zhu to J. Ng, dated December 4, 2003) concerning the preliminary results of monitoring studies for PBDEs in indoor air and ambient air conducted in Ottawa, Ontario, Canada.

Helleday, T., Tuominen, K.L., Bergman, A. and Jenssen, D. 1999. Brominated flame retardants induce intragenic recombination in mammalian cells. *Mutat. Res.* 439: 137–147.

Henry, B., Grant, S.G., Klopman, G. and Rosenkranz, H.S. 1998. Induction of forward mutations at the thymidine kinase locus of mouse lymphoma cells: evidence for electrophilic and non-electrophilic mechanisms. *Mutat. Res.* 397: 313–335 [secondary report of results from McGregor et al., 1988].

Hoberman, A.M., Lochry, E.A., Pinkerton, M.N. and Christian, M.S. 1998. Comparison of the developmental toxicity of octabromodiphenyloxide and pentabromodiphenyl oxide in Crl: CD (SD) BR rats. *Toxicologist* 64(8): 254 (abstract).

Hori, S., Akutsu, K., Oda, H., Nakazawa, H., Matsuki, Y. and Makino, T. 2002. Development of an analysis method for polybrominated diphenyl ethers and their levels in Japanese human mother's milk. *Organohalogen Compd.* 58: 245–248.

Huff, J.E., Eustis, S.L. and Haseman, J.K. 1989. Occurrence and relevance of chemically induced benign neoplasms in long-term carcinogenicity studies. *Cancer Metastasis*, 8: 1–21 [cited in IPCS, 1994].

Huwe, J.K., Lorentzen, M., Thuresson, K. and Bergman, A. 2002. Analysis of mono- to decabrominated diphenyl ethers in chickens at the part per billion level. *Chemosphere* 46: 635–640.

Ikonomou, M.G., Crewe, N., He, T. and Fischer, M. 1999. Polybrominated-diphenyl-ethers in biota samples from coastal British Columbia, Canada. *Organohalogen Compd.* 40: 341–345.

Ikonomou, M.G., Rayne, S., Fischer, M., Fernandez, M.P. and Cretney, W. 2002. Occurrence and congener profiles of polybrominated diphenyl ethers (PBDEs) in environmental samples from coastal British Columbia, Canada. *Chemosphere* 46: 649–663.

International Research and Development Corporation. 1977. Thirteen week feeding study in rats. Sponsor: Great Lakes Chemical Corporation. Published in U.S. Environmental Protection

Agency. 2000. Thirty-one 1,2-bis(tribromophenoxy)ethane studies, seven pentabromodiphenyl oxide studies and nine octabromodiphenyl oxide studies, with cover letter dated 11/28/88 (NTIS/OTS0517355; Document No. 86-890000045).

IPCS (International Programme on Chemical Safety). 1994. Brominated diphenyl ethers. World Health Organization, Geneva (Environmental Health Criteria 162).

ISC Chemicals Ltd. 1977. Tardex 50 Ames test. Unpublished report, Consultox Laboratories Ltd. (Project No. CL 77: 178) [cited in European Communities, 2000].

Jacobs, M.N., Covaci, A. and Schepens, P. 2002. Investigation of selected persistent organic pollutants in farmed Atlantic salmon (*Salmo salar*), salmon aquaculture feed, and fish oil components of the feed. *Environ. Sci. Technol.* 36: 2797–2805.

Jansson, B., Andersson, R., Asplund, L., Litzen, K., Nylund, K., Sellstrom, U., Uvemo, U., Wahlberg, C., Wideqvist, U., Odsjo, T. and Olsson, M. 1993. Chlorinated and brominated persistent organic compounds in biological samples from the environment. *Environ. Toxicol. Chem.* 12: 1163–1174.

Johnson, A. and Olson, N. 2001. Analysis and occurrence of polybrominated diphenyl ethers in Washington State freshwater fish. *Arch. Environ. Contam. Toxicol.* 41: 339–344.

Jones, K.C., Alcock, R.E., Kalantzi, O.I., Thomas, G.O., Asplund, L. and Kierkegaard, A. 2001. Environmental measurements and the global distribution of PBDEs (abstract). *In: Abstracts of the 2nd International Workshop on Brominated Flame Retardants, May 14–16, Stockholm, Sweden.* AB Firmatryck, Stockholm.

Kalk. 1982. [CFK Bromkal(R)-fire protection equipment.] Kalk Chemical Factory, Cologne (Information Sheet 3000-7/82) (in German) [cited in IPCS, 1994].

Kitchin, K.T. and Brown, J.L. 1994. Dose–response relationship for rat liver DNA damage caused by 49 rodent carcinogens. *Toxicology* 88: 31–49.

Kitchin, K.T., Brown, J.L. and Kulkarni, P. 1992. Predictive assay for rodent carcinogenicity using *in vivo* biochemical parameters: operational characteristics and complementarity. *Mutat. Res.* 266: 253–272 [cited in IPCS, 1994].

Kitchin, K.T., Brown, J.L. and Kulkarni, A.P. 1993. Predicting rodent carcinogenicity of halogenated hydrocarbons by *in vivo* biochemical parameters. *Teratogen. Carcinogen. Mutagen.* 13: 167–184.

Knoth, W., Mann, W., Meyer, R. and Nebhuth, J. 2002. Polybrominated diphenylether in house dust. *Organohalogen Compd.* 58: 213–216.

Kociba, R.J., Frauson, L.O., Humiston, C.G., Norris, J.M., Wade, C.E., Lisowe, R.W., Quast, J.F., Jersey, G.C. and Jewett, G.L. 1975a. Results of a two-year dietary feeding study with decabromodiphenyl oxide (DBDPO) in rats. Dow Chemical Company, Midland, Michigan (unpublished report submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Kociba, R.J., Frauson, L.O., Humiston, C.G., Norris, J.M., Wade, C.E., Lisowe, R.W., Quast, J.F., Jersey, G.C. and Jewett, G.L. 1975b. Results of a two-year dietary feeding study with decabromodiphenyl oxide (DBDPO) in rats. *Combust. Toxicol.* 2: 267–285 [cited in IPCS, 1994].

Kopp, A. 1990. [Documentation on fire-proofing agents containing bromine.] Nature Conservation and Nuclear Safety, Ministry of Environment, Bonn (report to the European Economic Community, Brussels) (in German) [cited in IPCS, 1994].

Kruger, C. 1988. [Polybrominated biphenyls and polybrominated diphenyl ethers — detection and quantification in selected foods.] Thesis, University of Munster, Munster (in German) [cited in IPCS, 1994].

Laws, S.C., Ferrell, J.M., Hedge, J.M., Crofton, K.M., Cooper, R.L. and Stoker, T.E. 2003. The effects of DE-71, a commercial polybrominated diphenyl ether mixture, on female pubertal development and thyroid function. *Toxicologist* 72(S-1): 136 (abstract).

LeBoeuf, R.A., Kerckaert, G.A., Aardema, M.J., Gibson, D.P., Brauninger, R. and Isfort, R.J. 1996. The pH 6.7 Syrian hamster embryo cell transformation assay for assessing the carcinogenic potential of chemicals. *Mutat. Res.* 356: 85–127.

Leonards, P.E.G., Santillo, D., Brigden, K., Van der Veen, I., Hesselings, J.V., DeBoer, J. and Johnston, P. 2001. Brominated flame retardants in office dust samples (abstract). *In: Abstracts of the 2nd International Workshop on Brominated Flame Retardants, May 14–16, Stockholm, Sweden.* AB Firmatryck, Stockholm.

Loganathan, B.G., Kannan, K., Watanabe, I., Dawano, M., Irvine, K., Kumar, S. and Sikka, H.C. 1995. Isomer-specific determination and toxic evaluation of polychlorinated biphenyl, polychlorinated/brominated dibenzo-p-dioxins and dibenzofurans, polybrominated biphenyl ethers, and extractable organic halogen in carp from the Buffalo River, New York. *Environ. Sci. Technol.* 29: 1832–1838.

Luckey, F., Fowler, B. and Litten, S. 2001. Establishing baseline levels of polybrominated diphenyl ethers in Lake Ontario surface waters (abstract). *In: Abstracts of the 2nd International Workshop on Brominated Flame Retardants, May 14–16, Stockholm, Sweden.* AB Firmatryck, Stockholm.

Luross, J.M., Alae, M., Sergeant, D.B., Cannon, C.M., Whittle, D.M., Solomon, K.R. and Muir, D.C.G. 2002. Spatial distribution of polybrominated diphenyl ethers and polybrominated biphenyls in lake trout from the Laurentian Great Lakes. *Chemosphere* 46: 665–672.

MA Bioservices Inc. 1998. Final report: bacterial reverse mutation assay of decabromodiphenyl oxide, with cover letter dated 9/14/98 (NTIS/OTS0559516; Document No. 86980000181).

MacPhail, R., Farmer, J.D., Padnos, B.K. and Crofton, K.M. 2003. Lack of effect of perinatal exposure to a polybrominated diphenyl ether mixture (DE-71) on the habituation of motor activity in adult rats. *Toxicologist* 72(S-1): 123 (abstract).

Manchester-Neesvig, J.B., Valters, K. and Sonzogni, W.C. 2001. Comparison of polybrominated diphenyl ethers (PBDEs) and polychlorinated biphenyls (PCBs) in Lake Michigan salmonids. *Environ. Sci. Technol.* 35: 1072–1077.

Matscheko, N., Tysklind, M., DeWit, C., Bergek, S., Andersson, R. and Sellstrom, 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 earthworms. *Environ. Toxicol. Chem.* 21(12): 2515–2525.

Matthews, E.J., Spalding, J.W. and Tennant, R.W. 1993. Transformation of BALB/c-3T3 cells: transformation responses of 168 chemicals compared with mutagenicity in *Salmonella* and carcinogenicity in rodent bioassays. *Environ. Health Perspect.* 101(Suppl. 2): 347–482.

McGregor, D.B., Brown, A., Cattanaach, P., Edwards, I., McBride, D., Riach, C. and Caspary, W.J. 1988. Responses of the L5178Y tk+/tk- mouse lymphoma cell forward mutation assay. *Environ. Mol. Mutagen.* 12: 85–154.

Meironyte, D., Bergman, A. and Noren, K. 1998. Analysis of polybrominated diphenyl ethers in human milk. *Organohalogen Compd.* 35: 387–390.

Meironyte Guvenius, D., Bergman, A. and Noren, K. 2002. Occurrence and pre-and postnatal transfer of PBDEs, PCBs and OH-PCBs in humans. *Organohalogen Compd.* 55: 271–274.

Microbiological Associates Inc. 1996a. Chromosome aberrations in human peripheral blood lymphocytes with pentabromodiphenyl oxide, with cover letter dated 01/08/97 (NTIS/OTS0001284; Document No. FYI-OTS-0197-1284).

Microbiological Associates Inc. 1996b. Pentabromodiphenyl oxide (PBDPO): Chromosome aberrations in human peripheral blood lymphocytes, with cover letter dated 01/08/97 (EPA/OTS; NTIS/OTS0573566; Document No. 86970000372).

Microbiological Associates Inc. 1996c. Bacterial reverse mutation assay of octabromodiphenyl oxide, with cover letter dated 09/30/96 (NTIS/OTS0001279; Document No. FYI-OTS-1096-1279).

Microbiological Associates Inc. 1996d. Final report, bacterial reverse mutation assay with octabromodiphenyl oxide, with cover letter dated 9/25/96 (NTIS/OTS0558804; Document No. 86960000603).

Moisey, J., Simon, M., Wakeford, B., Weseloh, D.V. and Norstrom, R.J. 2001. Spatial and temporal trends of polybrominated diphenyl ethers detected in Great Lakes herring gulls, 1981–2000 (abstract). *In: Abstracts of the 2nd International Workshop on Brominated Flame Retardants*, May 14–16, Stockholm, Sweden. AB Firmatryck, Stockholm.

Myrh, B., McGregor, D., Bowers, L., Riach, C., Brown, A.G., Edwards, I., McBride, D., Martin, R. and Caspary, W.J. 1990. L5178Y mouse lymphoma cell mutation assay results with 41 compounds. *Environ. Mol. Mutagen.* 16(Suppl. 18): 138–167 [secondary presentation of results from McGregor et al., 1988].

Norris, J.M., Ehrmantraut, J.W., Gibbons, C.L., Kociba, R.J., Schwetz, B.A., Rose, J.Q., Humiston, C.G., Jewett, G.L., Crummett, W.B., Gehring, P.J., Tirsell, J.B. and Brosier, J.S. 1973. Toxicological and environmental factors involved in the selection of decabromodiphenyl oxide as a fire retardant chemical. *Appl. Polymer Symp.* 22: 195–219 [cited in IPCS, 1994].

Norris, J.M., Ehrmantraut, J.W., Gibbons, C.L., Kociba, R.J., Schwetz, B.A., Rose, J.Q., Humiston, C.G., Jewett, G.L., Crummett, W.B., Gehring, P.J., Tirsell, J.B. and Brosier, J.S. 1974. Toxicological and environmental factors involved in the selection of decabromodiphenyloxide as a fire retardant chemical. *J. Fire Flamm. Combust. Toxicol.* 1: 52–77.

Norris, J.M., Ehrmantraut, J.W., Kociba, R.J., Schwetz, B.A., Rose, J.Q., Humiston, C.G., Jewett, G.L., Crummett, W.B., Gehring, P.J., Tirsell, J.B. and Brosier, J.S. 1975a. Evaluation of decabromodiphenyloxide as a flame-retardant chemical. *Chem. Hum. Health Environ.* 1: 100–116 [cited in IPCS, 1994].

Norris, J.M., Kociba, R.J., Humiston, C.G. and Gehring, P.J. 1975b. The toxicity of decabromodiphenyloxide and octabromodiphenyl as determined by subacute and chronic dietary feeding studies in rats. *Toxicol. Appl. Pharmacol.* 33(1): 170 (abstract) [cited in IPCS, 1994].

Norris, J.M., Kociba, R.J., Schwetz, B.A., Rose, J.Q., Humiston, C.G., Jewett, G.L., Gehring, P.J. and Mailhes, J.B. 1975c. Toxicology of octabromodiphenyl and decabromodiphenyloxide. *Environ. Health Perspect.* 11: 153–161 [cited in IPCS, 1994].

- Norstrom, 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 in Great Lakes herring gull eggs. *Environ. Sci. Technol.* 36: 4783–4789.
- NTP (National Toxicology Program). 1986. Toxicology and carcinogenesis studies of decabromodiphenyl oxide (CAS No. 1163-19-5) in F344/N rats and B6C3F1 mice (feed studies). U.S. Department of Health and Human Services, Research Triangle Park, North Carolina (Technical Report Series No. 309) [cited in IPCS, 1994].
- Ohta, S., Ishizuka, D., Nishimura, H., Nakao, T., Aozasa, O., Shimidzu, Y., Ochiai, F., Kida, T., Nishi, M. and Miyata, H. 2002. Comparison of polybrominated diphenyl ethers in fish, vegetables, and meats and levels in human milk of nursing women in Japan. *Chemosphere* 46: 689–696.
- Olsson, A., Vitinsh, M., Plikshs, M. and Bergman, A. 1999. Halogenated environmental contaminants in perch (*Perca fluviatilis*) from Latvian coastal areas. *Sci. Total Environ.* 239: 19–30.
- Papke, O., Bathe, L., Bergman, A., Furst, P., Guvenius, D.M., Herrmann, T. and Noren, K. 2001. Determination of PBDEs in human milk from the United States. *Organohalogen Compd.* 52: 197–200.
- Pettersson, A., Westberg, H., Engwall, M. and Ohlson, C.G. 2001. Concentrations in air and dust of polybrominated diphenyl ethers and tetrabromobisphenol A (abstract). *In: Abstracts of the 2nd International Workshop on Brominated Flame Retardants, May 14–16, Stockholm, Sweden.* AB Firmatryck, Stockholm.
- Pharmakon Research International Inc. 1984. Initial submission: acute oral toxicity study in rats (14 day) of Saytex 115 (pentabromodiphenyloxide) (NTIS/OTS0000972; Document No. FYI-OTS-0794-0972).
- Rayne, S., Ikonou, M.G. and Antcliffe, B. 2003. Rapidly increasing polybrominated diphenyl ether concentrations in the Columbia River system from 1992 to 2000. *Environ. Sci. Technol.* 37(13): 2847–2854. Supporting information available at <http://pubs.acs.org/subscribe/journals/esthag/suppinfo/es0340073/es0340073si20030325_014437.pdf>.
- Rice, C.P., Chernyak, S.M., Begnoche, L., Quintal, R. and 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.
- Rudel, R.A., Camann, D.E., Spengler, J.D., Korn, L.R. and Brody, J.G. 2003. Phthalates, alkylphenols, pesticides, polybrominated diphenyl ethers, and other endocrine disrupting

compounds in indoor air and dust. *Environ. Sci. Technol.* 37(20): 4543–4553. Supporting information available at http://pubs.acs.org/subscribe/journals/esthag/supinfo/es0264596/es0264596si20030910_033657.pdf.

Rutter, H.A. and Machotka, S. 1979. Decabromodiphenyloxyde: 13-week subchronic feeding study — mice. Final report. Hazleton Laboratories America Inc., Vienna, VA (unpublished report to Tracor Jitco, Rockville, MD, submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Ryan, J.J. Undated. Unpublished data: concentrations of brominated diphenyl ether congeners in 40 composite of total diet food samples collected in the winter of 1998 in Whitehorse. Health Canada.

Ryan, J.J. and Patry, B. 2000. Determination of brominated diphenyl ethers (BDEs) and levels in Canadian human milks. *Organohalogen Compd.* 47: 57–60.

Ryan, J.J. and Patry, B. 2001a. Body burdens and food exposure in Canada for polybrominated diphenyl ethers (BDEs). *Organohalogen Compd.* 51: 226–229.

Ryan, J.J. and Patry, B. 2001b. Body burdens and exposure from food for polybrominated diphenyl ethers (BDEs) in Canada (abstract). *In: Abstracts of the 2nd International Workshop on Brominated Flame Retardants, May 14–16, Stockholm, Sweden.* AB Firmatryck, Stockholm.

Ryan, J.J., Patry, B., Mills, P. and Beaudoin, N.G. 2002a. Recent trends in levels of brominated diphenyl ethers (BDEs) in human milks from Canada (abstract). Unpublished report from the 4th Annual Workshop on Brominated Flame Retardants in the Environment, June 17–18, Burlington, Ontario.

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

Schwetz, B.A., Smith, F.A., Nitschke, K.D., Humiston, C.G., Jersey, G.C. and Kociba, R.J. 1975. Results of a reproduction study in rats maintained on diets containing decabromodiphenyloxyde. Dow Chemical Company, Midland, Michigan (unpublished report No. HET K-47298-(14), submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Sellstrom, U., Jansson, B., Kierkegaard, A., de Wit, C., Odsjo, T. and Olsson, M. 1993. Polybrominated diphenyl ethers (PBDE) in biological samples from the Swedish environment. *Chemosphere* 26(9): 1703–1718.

Sellstrom, U., Kierkegaard, A., DeWit, C. and Jansson, B. 1998. Polybrominated diphenyl ethers and hexabromocyclododecane in sediment and fish from a Swedish river. *Environ. Toxicol. Chem.* 17(6): 1065–1072.

Shoichet, A. and Ehrlich, K. 1977. Mutagenicity testing of HFO 102 (unpublished proprietary report from Gulf South Research Institute, New Orleans, Louisiana, to Hexel Fine Organics) (report submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Sjodin, A., Carlsson, H., Thuresson, K., Sjolín, S., Bergman, A. and Ostman, C. 2001. Flame retardants in indoor air at an electronics recycling plant and other work environments. *Environ. Sci. Technol.* 35(3): 448–454.

Sparschu, G.L., Kociba, R.J. and Clashman, A. 1971. Results of 30 day rat dietary feeding studies on octabromobiphenyl SA-1902 and decabromodiphenyl oxide SA-1892.1. Dow Chemical Company, Midland, Michigan (unpublished report submitted to the World Health Organization by the Brominated Flame Retardant Industry Panel) [cited in IPCS, 1994].

Stoker, T.E., Ferrell, J., Hedge, M.J., Crofton, K.M., Cooper, R.L. and Laws, S.C. 2003. Assessment of DE-71, a commercial polybrominated diphenyl ether (PBDE) mixture, in the EDSP male pubertal protocol. *Toxicologist* 72(S-1): 135–136 (abstract).

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(6): 1078–1083.

Strandman, T., Koistinen, J. and Vartiainen, T. 2000. Polybrominated diphenyl ethers (PBDEs) in placenta and human milk. *Organohalogen Compd.* 47: 61–64.

Taylor, M.M., Hedge, J.M., DeVito, M.J. and Crofton, K.M. 2002. Perinatal exposure to a polybrominated diphenyl ether mixture (DE-71) disrupts thyroid hormones but not neurobehavioral development. *Toxicologist* 66(1-S): 133 (abstract).

Taylor, M.M., Hedge, J.M., Gilbert, M.E., DeVito, M.J. and Crofton, K. 2003. Perinatal exposure to a polybrominated diphenyl ether mixture (DE-71): disruption of thyroid homeostasis and neurobehavioral development. *Toxicologist* 72(S-1): 124 (abstract).

Thomsen, C., Leknes, H., Lundanes, E. and Becher, G. 2001. Brominated flame retardants in laboratory air. *J. Chromatogr. A* 923: 299–304.

Thuvander, A. and Darnerud, P.O. 1999. Effects of polybrominated diphenyl ether (PBDE) and polychlorinated biphenyl (PCB) on some immunological parameters after oral exposure in rats and mice. *Toxicol. Environ. Chem.* 70: 229–242.

U.S. EPA (U.S. Environmental Protection Agency). 1986. Brominated diphenyl ethers. Chemical hazard information profile. Washington, D.C. [cited in IPCS, 1994].

U.S. EPA (U.S. Environmental Protection Agency). 1989. Letter from Director Office of Toxic Substances, Washington, D.C., to Great Lakes Chemical Corporation, dated 07/27/89 [cited in IPCS, 1994].

U.S. EPA (U.S. Environmental Protection Agency). 1997. Exposure factors handbook. Vol. 2. Chapter 14. Available at <<http://www.epa.gov/ncea/exposfac.htm>>, accessed May 2002 (NTIS/PB98-124233).

Viberg, H. 2002. Personal communication. Comments regarding abstract from the 2nd International Workshop on Brominated Flame Retardants 2001 [Viberg et al., 2001b] to A. Lam, Existing Substances Division, Health Canada, Ottawa, dated 11/29/02.

Viberg, H., Fredriksson, A., Jacobsson, E., Ohrn, U. and Eriksson, P. 2000. Developmental neurotoxic effects of 2,2',4,4',5-pentabromodiphenyl ether (PBDE99) in the neonatal mouse. *Toxicologist* 54(1): 290 (abstract).

Viberg, H., Fredriksson, A., Jakobsson, E., Ohrn, U. and Eriksson, P. 2001a. Brominated flame-retardant: uptake, retention and developmental neurotoxic effects of decabromo-diphenyl ether (PBDE209) in the neonatal mouse. *Toxicologist* 61: 1034 (abstract).

Viberg, H., Fredriksson, A., Jakobsson, E., Orn, U. and Eriksson, P. 2001b. Brominated flame retardants: uptake, retention and developmental neurotoxic effects of decabromodiphenyl ether (PBDE209) in the neonatal mouse (abstract). *In*: Abstracts of the 2nd International Workshop on Brominated Flame Retardants, May 14–16, Stockholm, Sweden. AB Firmatryck, Stockholm.

Viberg, H., Fredriksson, A. and Eriksson, P. 2002a. Developmental exposure to a brominated flame-retardant 2,2',4,4',5,5'-hexabromodiphenyl ether (PBDE 153) affects behaviour and cholinergic nicotinic receptors in brain of adult mice. *Toxicologist* 66(1-S): 132 (abstract).

Viberg, H., Fredriksson, A. and Eriksson, P. 2002b. 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: 104–107.

Viberg, H., Fredriksson, A., Jakobsson, E., Orn, U. and Eriksson, P. 2003. Neurobehavioral derangements in adult mice receiving decabrominated diphenyl ether (PBDE 209) during a defined period of neonatal brain development. *Toxicol. Sci.* 76: 112–120.

Von Meyerinck, L., Hufnagel, B., Schmoltdt, A. and Benthe, H.F. 1990. Induction of rat liver microsomal cytochrome P-450 by the pentabromodiphenyl ether Bromkal 70 and half lives of its components in the adipose tissue. *Toxicology* 61: 259–274 [cited in IPCS, 1994].

Wakeford, B.J., Simon, M.J., Elliott, J.E. and Braune, B.M. 2002. Analysis of polybrominated diphenyl ethers (BDEs) in wildlife tissues — Canadian Wildlife Service contributions. Unpublished report from the 4th Annual Workshop on Brominated Flame Retardants in the Environment, June 17–18, Burlington, Ontario.

Wenning, R.J. 2002. Uncertainties and data needs in risk assessment of three commercial polybrominated diphenyl ethers: probabilistic exposure analysis and comparison with European Commission results. *Chemosphere* 46: 779–796.

Wijesekera, R., Halliwell, C., Hunter, S. and Harrad, S. 2002. A preliminary assessment of UK human exposure to polybrominated diphenyl ethers (PBDEs). *Organohalogen Compd.* 55: 239–242.

Wil Research Laboratories Inc. (a subsidiary of Great Lakes Chemical Corporation). 1984. 90-day dietary study in rats with pentabromodiphenyl oxide (DE-71), project number WIL-12011. Published in U.S. Environmental Protection Agency. 2000. Thirty-one 1,2-bis(tribromophenoxy)ethane studies, seven pentabromodiphenyl oxide studies and nine octabromodiphenyl oxide studies, with cover letter dated 11/28/88 (NTIS/OTS0517355; Document No. 86-890000045).

Zegers, B.N., Lewis, W.E., Tjoen-A-Choy, M.R., Smeenk, C., Siebert, U. and Boon, J.P. 2001. Levels of some polybrominated diphenyl ether (PBDE) flame-retardants in animals of different trophic levels of the North Sea food web. *Organohalogen Compd.* 52: 18–21.

Zeiger, E., Anderson, B., Haworth, S., Lawlor, T., Mortelmans, K. and Speck, W. 1987. *Salmonella* mutagenicity tests: III. Results from the testing of 255 chemicals. *Environ. Mutagen.* 9 (Suppl. 9): 1–109 [cited in European Communities, 2000].

Zhou, T., Taylor, M.M., DeVito, M.J. and Crofton, K.M. 2000. Thyroid hormone disruptive effects of brominated diphenyl ethers following developmental exposure. *Toxicologist* 54(1): 260–261 (abstract).

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., DeVito, M.J. and Crofton, K.M. 2002. Developmental exposure to brominated diphenyl ethers results in thyroid hormone disruption. *Toxicol. Sci.* 66: 105–116.

