Michigan Department of Environmental Quality

POLYBROMINATED DIPHENYL ETHERS: A SCIENTIFIC REVIEW WITH RISK CHARACTERIZATION AND RECOMMENDATIONS

Prepared by

The Toxics Steering Group
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EXECUTIVE SUMMARY

This document was written in response to a request from the Michigan Department of Environmental Quality (MDEQ) management for information about Polybrominated Diphenyl Ethers (PBDEs) and is an update to the January 2007 version of the report. The information was needed to make decisions regarding placement of PBDEs on the Critical Materials Register (CMR) and the MDEQ's response to proposed legislation to ban PBDEs in Michigan.

This document includes the following information about PBDEs:

- Description and Use
- Toxicity and Toxicokinetics
- Environmental Fate and Chemical Characteristics
- Levels in the Environment
- Potential Risks to Humans
- Regulatory and Legislative Actions
- Conclusions and Recommendations

The information presented is not a complete summary of all available data, but focuses on the information that will be most helpful to the decision making process regarding the CMR and proposed legislation. The data cited includes original research articles, as well as review summaries.

PBDEs are brominated fire retardants (BFRs) used primarily in plastics and textile coatings. In this class of compounds, 2-10 bromines are attached to the diphenyl ether molecule. PBDEs are of significant environmental concern because they are toxic, bioaccumulative, and persistent. Levels in humans and wildlife are increasing exponentially. The primary commercial products of PBDEs are Penta-, Octa-, and Deca-BDEs. Each is a mixture of specific PBDE chemicals or congeners. For example, commercial Penta-BDE contains 0.1% Tri-BDE, 24-38% Tetra-BDE, 50-62% Penta-BDE, and 4-8% Hexa-BDE. The 209 possible PBDE congeners are identified in the International Union of Pure and Applied Chemistry (IUPAC) numbering system, which arranges them in ascending numerical order of the degree of bromination. For example, BDE-99 is 2,2',4,4',5-Penta-BDE.

Toxicity

Toxicity data for PBDEs are limited. Exposure of laboratory animals to PBDEs has resulted in histopathological changes to the liver, neurodevelopmental effects in developing animals, and/or reductions in thyroid hormone levels. The United States Environmental Protection Agency (U.S. EPA) currently uses the induction of liver enzymes or other effects in the liver as the critical effect in the derivation of reference doses (RfDs) for three of the PBDE congeners. Draft U.S. EPA RfD documents are currently under review. However, more recent studies suggest that effects on the developing brain may be as, or more, sensitive than effects on the liver. Deca-BDE is the only PBDE congener that has been tested for carcinogenicity. Some evidence of carcinogenicity was found for rats following exposure to very high levels in feed. Overall, the lower brominated congeners and mixtures appear to be more toxic than the higher brominated compounds.

Some PBDE congeners exhibit toxicity similar to dioxins. Dioxins have high affinity for the Aryl Hydrocarbon (Ah receptor). The cascade of toxic effects caused by dioxin begins with binding to the Ah receptor. Dioxins also significantly induce ethoxyresorufin-o-deethylase (EROD), which represents an ability to induce Cytochrome P450 1A liver enzymes. Studies have shown that some of the PBDE congeners have a low-to-moderate binding affinity for the Ah receptor and a weak potential to induce EROD, whereas other congeners exhibit no binding affinity for the Ah receptor or have an antagonistic effect. A recent study concluded that the concentrations of PBDEs currently detected in biota contribute negligibly to dioxin-like activity compared with other contaminants found in biota.

Toxicokinetics

Limited toxicokinetic data are available in the scientific literature on PBDEs. There is evidence in animals and humans that PBDEs are bioavailable, although the lower brominated congeners (Tetra- through Hexa-BDEs) appear to be more readily absorbed than the higher brominated congeners (Hepta- through Deca-BDEs). The lower brominated congeners appear to distribute preferentially to lipid rich tissues, especially adipose tissue. The higher brominated congeners once absorbed appear to be distributed to more highly perfused tissues, with less accumulation in adipose tissue. Metabolism has been directly indicated or strongly suggested, has some species specificity, and occurs more readily for the higher brominated congeners. Oxidative debromination has been observed with some PBDEs resulting in hydroxylated and sometimes methoxylated metabolites. Fecal excretion appears to be the predominant elimination pathway in rats. Metabolites are found in the bile and urine. Metabolism and urinary excretion have been demonstrated to be an equally important elimination mechanism in mice.

The identification of hydroxylated PBDE residues in blood suggests that PBDEs are metabolized in many species. Evidence suggests that some PBDEs may affect hormonal systems or neurodevelopment via formation of active metabolites.

Although previously thought to be biologically unavailable, recent studies indicate some bioavailability for Deca-BDE. A recent study indicates evidence of limited bioavailability of Deca-BDE in Carp. Seven apparent debrominated products of Deca-BDE accumulated in whole fish and liver tissues. A study in mice demonstrated uptake in the brain, liver, and heart after oral exposure to ^{14}C-labeled Deca-BDE. Several recent studies have identified detectable levels of Deca-BDE in human tissues.

Environmental Fate and Chemical Characteristics

Based on the chemical characteristics of PBDEs, they are expected to be persistent and bioaccumulative in the environment. The half-life of PBDEs in soil and water was estimated to be 150 days, and 600 days in sediment. Studies show that environmental degradation of PBDEs occurs by both photolytic and bacterial means. The more highly brominated congeners lose bromine atoms more quickly than lower brominated congeners. The rates of degradation are dependent on the solvent, light source, and substrates involved. In laboratory studies, Deca-BDE did degrade more quickly than lower brominated compounds, however the rate of degradation and degradation products generated in the environment are not well characterized. PBDEs are highly lipophilic indicated by their high log K_{ow} values ranging from 5.9-7.9. The lipophilic nature of these chemicals indicates they would likely bioaccumulate in animals.

Levels in the Environment

Levels in Biota and Food

PBDEs have been detected in aquatic and terrestrial biota from numerous locations around the globe. The most prevalent congeners were BDE-47, BDE-99, and BDE-100. Concentrations in several species of biota have increased dramatically between 1980 and the present. Within some geographic regions, higher concentrations have been observed in relatively warmer climates. Generally, North American biota appears to have higher concentrations than European biota.

PBDE concentrations have been found to be the highest in fish, followed by meat, and then dairy products. Great Lakes fish have been observed to have relatively high concentrations of PBDEs compared to other foods. However, concentrations in milk and chicken may be considered substantial, given the total quantities of these items consumed by the public.

Deca-BDE had been detected in food and wildlife. Studies have shown that terrestrial animals (those feeding on land) may be more likely to bioaccumulate Deca-BDE as compared to aquatic feeding organisms. The limited data on Deca-BDE is in part caused by the fact that analytical labs have just recently (within the last several years) been able to quantify Deca-BDE. Furthermore, studies have shown that several species of animals readily metabolize Deca-BDE from the parent compound to lesser-brominated congeners. Debromination of Deca-BDE reduces or eliminates the presence of Deca-BDE, but results in higher concentrations of the lower brominated congeners, many of which are more toxic than Deca-BDE.

Levels in Humans

Data on concentrations of PBDEs in human blood, breast milk, and adipose tissue have consistently shown levels to be significantly higher in North America, compared to Europe or Japan. Levels found in the United States (U.S.) are the highest of all countries for which there are data and are about ten to 100 times greater than human tissue levels in Europe. Two recent studies of U.S. breast milk levels showed total PBDE concentrations ranged from 6.2-419 ng/g lipid in one study (Schecter et al., 2003) and 9.5-1,078 ng/g in another study (EWG, 2003). Typically, BDE-47 is found at the highest concentration in human tissue and comprises at least half of the total PBDEs. The next most abundant congener often detected is BDE-99. Human samples from Japan, Europe, and North America during the period of 1970-2002, show that BDE-47 comprised about 50% of the total PBDEs, followed next by BDE-153 at about 20%,

and then BDE-99, BDE-100, and BDE-154 at lower percentages (Hites, 2004). Limited data are available on levels of Deca-BDE in humans, as many studies have not included analysis for this congener, although it has been found in human blood, breast milk, and adipose tissue in a few studies. Levels of Deca-BDE in human tissues are typically lower than other congeners, with one study reporting a median concentration of 0.4 ng/g lipid in breast milk (Northwest Environment Watch, 2004) and another median concentration of 2.3 ng/g lipid in whole blood (Schecter et al., 2005).

Temporal trends of PBDEs in human tissues show levels in North America are increasing significantly over time. Data on blood levels from 1959-1966 showed no detectable levels of BDE-47 compared to levels of <10-511 ng/g lipid in blood samples from 1997-1999 (Petreas et al., 2003). PBDE levels in breast milk also show similar increases over time and appear to be doubling every 2-5 years in North America (Betts, 2002).

Levels in Environmental Media

PBDEs have been found in ambient air, lakes, rivers, soils, and sediments as well as in the indoor environment. Average concentrations of total PBDEs in ambient air from four sites in the Great Lakes basin, and three sites in Indiana, Arkansas, and Louisiana ranged from 5.5-100 pg/m^3, with the highest concentration found in the urban area of Chicago, Illinois (Strandberg et al., 2001; Hoh and Hites, 2005). At the Chicago site, concentrations increased from 52 pg/m^3 during 1997-1999, to 100 pg/m^3 during 2002-2003. PBDE levels measured in the Lake Michigan water column in 1997-1999 ranged from 31-158 pg/L compared to 6 pg/L in Lake Ontario (Hale et al., 2003). PBDEs have also been found in sediments from freshwater tributaries and lakes, as well as in sewage sludge samples. Deca-BDE is the predominant congener found in most sediment, including those of the Great Lakes, where average concentrations ranged from a low of 11 ng/g in Lake Superior to a high of 227 ng/g in Lake Ontario (Song et al., 2004, 2005b; Zhu and Hites, 2005). PBDE concentrations in sewage sludge samples from North America are significantly higher than those found in Europe (Hale et al., 2003).

PBDEs are also found in the indoor environment, including indoor air and house dust. Indoor air concentrations appear to be significantly higher than outdoor air concentrations, with one study showing indoor concentrations fifty times higher than the outdoors (Wilford et al., 2004b). PBDEs in house dust in North American have been found at levels ranging from 170-170,000 ng/g, with average concentrations of 4,600-12,000 ng/g. Typically Deca-BDE is found at the highest concentration in house dust, with BDE-47 and BDE-99 the other major contributors to the total PBDEs in this media.

Potential Risks to Humans

The Potential Risk Section consists of summaries of two risk assessments from the scientific literature (Hays and Pratt, 2006; McDonald, 2005) and a risk assessment conducted by the Toxics Steering Group (TSG) for this report. The TSG used a Margin of Exposure (MOE) approach to compare congener-specific human body burdens to estimate animal body burdens for specific congeners. The 2007 version of the report included MOE estimates for Deca-BDE, but those were withdrawn in this final version due to the significant uncertainties associated with quantifying risks for this congener. See the Potential Risk Section and Appendix C (Responses to Comments) for details. Specifically, a MOE is calculated by dividing the estimated animal body burden Lowest Observed Adverse Effect Level (LOAEL) by the human tissue levels.

Estimates of animal body burdens were calculated from the LOAELs reported in several animal toxicity studies for each of the following PBDE congeners: BDE-47, -99, and -153. The calculation used to estimate the body burden LOAEL is presented. Human tissue levels used to generate the MOEs were the lowest median, the highest median, and the highest body burden concentrations from the studies reviewed for this report. The uncertainties associated with the approach are identified. A MOE of 300 or greater is identified as posing a minimal level of risk to humans based on the information cited in the report. A significant concern for highly exposed individuals to BDE-47, -99, and -153 was identified based on the estimated ranges of MOEs. A range of MOEs was also estimated for total PBDEs suggesting a significant level of risk and concern for exposures to all PBDEs combined.

Regulatory and Legislative Action

Michigan

A MDEQ staff report recommends that Penta-, Octa-, and Deca-BDEs be placed on the CMR; the TSG PBDE Subcommittee supports that recommendation. The CMR is a list of substances which pose an environmental concern. All facilities with a non-sanitary wastewater discharge are required, by law, to report annually on their use and discharge of chemicals on the CMR.

House Bill 4406, was signed into law as Public Act 562 in 2004, and became effective January 3, 2005. Beginning on June 2, 2006, a person shall not manufacture, process, or distribute a product or material containing more than 1/10 of 1% of Penta-BDE. Senate Bill 1458 is a similar bill that addresses Octa-BDE; it was also signed into law in 2004 and became Public Act 526.

House Bill 5573, which proposes to ban Deca-BDE in a similar fashion, was introduced on January 24, 2006.

Other States, the U.S. EPA, and Related Information

California was the first state to ban the manufacture and commercial distribution of products containing more than 1/10 of 1% of Penta- or Octa-BDE. Bills to ban or regulate products containing PBDEs have also been adopted in Hawaii, New York, Illinois, Maryland, Oregon, and Maine. The U.S. EPA issued a draft Significant New Use Rule for Penta- and Octa-BDE on December 6, 2004. The U.S. EPA has included PBDEs in the High Production Volume Evaluation and Testing Programs and also in a pilot program for the Voluntary Children's Chemical Evaluation Program (VCCEP). The main U.S. manufacturer of Penta- and Octa-BDE voluntarily ceased production of Penta- and Octa-formulations at the end of 2004. Replacement chemicals must be adequately tested to assure they will not present unacceptable risks to human health and the environment. In 2006 the U.S. EPA also released the PBDE Project Plan.

Europe

In early 2003, the European Union (EU) adopted a directive, which banned the marketing and use of Penta- and Octa-BDE in all consumer products beginning August 15, 2004. In addition, a separate European-wide ban under the Restriction on Hazardous Substances, which has a specific focus on electronics, will eliminate all PBDEs in electronics by 2006. A risk assessment on Deca-BDE conducted by the EU is being evaluated to determine if Deca-BDE should be exempt from the electronics ban.

Conclusions and Recommendations

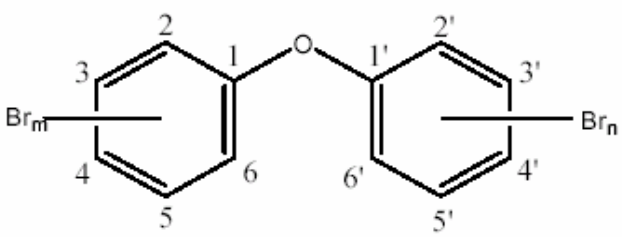
The updated conclusions and recommendations focus on Deca-BDE, since Penta- and Octa-BDEs were banned in 2006. Various concerns and uncertainties related to Deca-BDE are summarized, including its neurodevelopmental toxicity, significant potential for human exposures, and detectable levels in various biota including humans. The first recommendation is to support a legislative ban on Deca-BDE contingent on the availability of a safe alternative. Rationale is provided and includes various uncertainties and concerns, such as increasing trends of other PBDE congeners in humans, limited data on human tissue concentrations particularly in children, significant exposure potential for children, the potentially significant breakdown of Deca-BDE into the more toxic, lower brominated congeners, among others. The remaining recommendations are: investigate the efficacy of the legislative bans on Penta- and Octa-BDE; develop criteria when adequate toxicity studies are available and/or the U.S. EPA completes the draft RfDs; pursue development of educational materials aimed at reducing exposures in children; investigate the safety of replacements for PBDEs; pursue options for changing the U.S. chemical policy; and consider implementing some of the monitoring recommendations in the 2004 PBDE Draft Report.

INTRODUCTION

This document was written in response to a request from the MDEQ management for information about PBDEs. The information was needed to make decisions regarding placement of PBDEs on the CMR and the MDEQ's response to proposed legislation to ban PBDEs in Michigan. This report is an update of the Polybrominated Diphenyl Ethers: Background Paper 2004 Draft. An updated draft was released in May 2007 for external review. Comments were received, and those are presented in Appendix D; responses to those comments are presented in Appendix C. Based on the comments received and additional information published in the scientific literature, the quantitative risk assessment for Deca-BDE was withdrawn from the 2008 final report.

PBDEs are a class of BFRs, which are ubiquitously distributed in the environment. These compounds are of concern, since levels in biota, human tissues, and breast milk are increasing exponentially. In this class of compounds, 2-10 bromine atoms are attached to the diphenyl ether molecule. The number and arrangement of bromine atoms results in the possibility of 209 different PBDE compounds or congeners. Figure 1 presents the chemical structure for PBDEs.

Figure 1: Generalized Structure of PBDEs (where (m+n) = 2 to 10 bromines)



The 209 congeners for PBDEs are arranged in ascending numerical order using a numbering system that follows the International Union of Pure and Applied Chemistry (IUPAC) rules of constituent characterization in biphenyls. The resulting IUPAC numbers, such as BDE-99, are associated with a specific congener — in this case 2,2',4,4',5-Penta-BDE, and they are also referred to as IUPAC or Ballschmiter-Zell numbers. The IUPAC numbers are widely used for identifying individual congeners of PBDEs and also polybrominated biphenyls (PBBs). A representative group of PBDE conger IUPAC numbers is presented in Table 1.

Commercial products of PBDEs are also identified by registered trade names. For example, trade names for Penta-PBDE commercial products include DE-71, Bromkal 70, and Tardex 50.

Two additional trade names mentioned in this document are Bromkal 70-5DE (primarily 2,2',4,4'-Tetra-BDE; 2,2',4,4',5-Penta-BDE; and a small amount of 2,2',4,4',6-Penta-BDE) and Saytex 111 (an Octa-BDE product containing 6-9 bromines).

Commercial production of PBDEs began in the late 1970s. PBDEs are physically combined with the polymer material being treated (additive flame retardant) rather than chemically combined (reactive flame retardants). As a result, there is a possibility that PBDEs may diffuse out of the treated material to some extent.

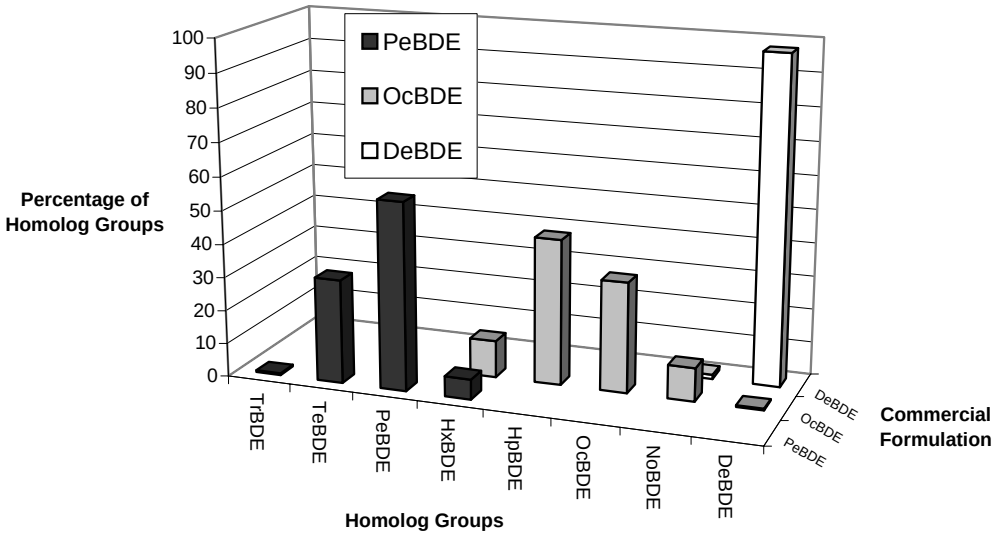
Table 1: IUPAC Numbers for Specific PBDE Congeners

IUPAC NUMBER	PBDE Congener
BDE-1	2-Mono-BDE
BDE-12	3,4-Di-BDE
BDE-15	4,4'-Di-BDE
BDE-17	2,2',4-Tri-BDE
BDE-25	2,3',4-Tri-BDE
BDE-28	2,4,4-Tri-BDE
BDE-30	2,4,6-Tri-BDE
BDE-33	2',3,4'-Tri-BDE
BDE-47	2,2',4,4'-Tetra-BDE
BDE-49	2,2',4,5'-Tetra-BDE
BDE-51	2,2',4,6'-Tetra-BDE
BDE-66	2,3',4,4'-Tetra-BDE
BDE-71	2,3',4',6-Tetra-BDE
BDE-75	2,4,4',6-Tetra-BDE
BDE-77	3,3',4,4'-Tetra-BDE
BDE-79	3,3',4,5'-Tetra-BDE
BDE-85	2,2',3,4,4'-Penta-BDE
BDE-99	2,2',4,4',5-Penta-BDE
BDE-100	2,2',4',4',6-Penta-BDE
BDE-119	2,3',4,4',6-Penta-BDE
BDE-138	2,2',3,4,4',5'-Hexa-BDE
BDE-140	2,2',3,4,4',6-Hexa-BDE
BDE-153	2,2',4,4',5,5'-Hexa-BDE
BDE-154	2,2',4,4',5,6'-Hexa-BDE
BDE-155	2,2',4,4',6,6'-Hexa-BDE
BDE-166	2,3,4,4',5,6'-Hexa-BDE
BDE-180	2,2',3,4,4',5,5'-Hepta-BDE
BDE-183	2,2',3,4,4',5',6-Hepta-BDE
BDE-190	2,3,3',4,4',5,6-Hepta-BDE
BDE-203	2,2',3,4,4',5,5',6-Octa-BDE
BDE-206	2,2',3,3',4,4',5,5',6,-Nona-BDE
BDE-209 (= Deca-BDE)	2,2',3,3',4,4',5,5',6,6'-Deca-BDE

PBDEs are used as fire retardants in plastics and textile coatings. Three commercial mixtures of PBDEs have been, and continue to be, produced: Deca-BDE, Octa-BDE, and Penta-BDE. These commercial products contain a mixture of various congeners. For example, commercial Penta-BDE contains 0.1% Tri-BDE, 24-38% Tetra-BDE, 50-62% Penta-BDE, and 4-8% Hexa-BDE. Commercial Octa-BDE contains 10-12% Hexa-BDE, 43-44% Hepta-BDE, 31-35% Octa-BDE, 9-11% Nona-BDE, and 0-1% Deca-BDE. Commercial Deca-BDE contains 0.3-3% Nona-BDE and 97-98% Deca-BDE (WHO, 1994). Percentages of the various homolog groups in each of the three commercial formulations are presented in Figure 2. In the U.S., PBDEs are only produced in Arkansas at the Albemarle Corporation (Magnolia, AR) and at the Great Lakes Chemical Corporation (Eldorado, AR) (ATSDR, 2004).

Figure 2: Percentages of Homolog Groups that Constitute Each of the Three Commercial Formulations (Penta-BDE, Octa-BDE, and Deca-BDE)

(Data graphic acquired from WHO, 1994)



The demand for Deca-BDE, Octa-BDE, and Penta-BDE in North America in 1999 was 24,300 tons; 1,375 tons; and 8,290 tons, respectively (Hale and Ciparis, 2003). The major uses of PBDEs in descending order of importance are: high-impact polystyrene, acrylonitrile-butadiene-styrene terpolymer (ABS), flexible polyurethane foam, textile coatings, wire and cable insulation, electronic connectors, and other interior parts of various products (WHO, 1994). About 40% of commercial Deca-BDE is used in high impact polystyrene applications, such as television and radio housings. Other significant uses of commercial Deca-BDE are in textile applications, such as polyester fiber additives and coatings for automobile fabric, tarpaulins, and tents. Commercial Octa-BDE is mainly used in the preparation of ABS, which is used in the manufacture of computer and business equipment housings. Commercial Octa-BDE is also used in adhesives and coatings. About 95% of commercial Penta-BDE is used in the

manufacture of flexible polyurethane foam used in furniture and upholstery, automobiles, and foam-based packaging (ATSDR, 2004).

PBDEs are released into the environment during their manufacture and use as additive flame retardants in thermoplastics in a wide range of products (WHO, 1994). Waste containing PBDEs may be incinerated as municipal waste, deposited in landfills, discharged to municipal sewage treatment plants, or emitted into the atmosphere.

TOXICOLOGY

Relative Toxicity

Since PBDEs have structures similar to other halogenated aromatic contaminants, such as polychlorinated biphenyls (PCBs) and dioxin, it has been proposed they may have a similar mechanism of action. Chen et al., (2001), demonstrated the ability of 12 PBDE congeners to induce EROD activity in assays using human, rat, and chick cells. Inactive were 4-6 congeners, depending on which cell line was being studied. The highest relative potencies found in humans (BDE-126), rats (BDE-126, 77, 119), and chicks (BDE-77, 126) were 10^{-4}, 10^{-4}, and 10^{-3}, respectively. Meerts et al., (1998), determined that seven BDE congeners acted as Ah receptor agonists, whereas, nine BDE congeners acted as antagonists when co-treated with tetrachlorodibenzo-p-dioxin (TCDD). Hanberg et al., (1991), determined that a commercial formulation of Penta-BDE induced EROD levels in rat hepatoma cells with a potency relative to 2,3,7,8-TCDD of 10^{-6}. Using the Calux bioassay, Behnisch et al., (2003), determined the potencies of 13 PBDE congeners relative to 2,3,7,8-TCDD ranged from 10^{-5} to 10^{-7}. Brown et al., (2004), determined that Deca-BDE had potency relative to 2,3,7,8-TCDD of 10^{-6} using the Calux bioassay.

Several studies have examined the potential for PBDEs to induce EROD activity in aquatic life. Chen et al., (2001), determined the ability of 12 PBDE congeners to induce EROD activity in rainbow trout cells. Six PBDE congeners were inactive. The highest potency relative to 2,3,7,8-TCDD was 10^{-4} for BDE-126, BDE-77 and BDE-119. Tjarnlund et al., (1998), determined that BDE-47 and BDE-99 caused a significant decrease in EROD activity when fed to rainbow trout. Kuiper et al., (2004), determined that DE-71 (commercial Penta-BDE), BDE-47, BDE-99, and BDE-153 reduced the induction of EROD activity by 2,3,7,8-TCDD in carp embryos (BDE-100 did not affect EROD induction). Bromkal 70-5DE showed weak dioxin-like activity and weak EROD induction activity in injected rainbow trout cells and in sticklebacks exposed to the PBDEs via their feed (Sellstrom et al., 1998).

Hornung et al., (1996), injected newly fertilized rainbow trout eggs with various polybrominated and polychlorinated compounds to determine their toxicity relative to the toxicity of 2,3,7,8-TCDD. The three PBDEs (BDE-47; BDE-85; and BDE-99) examined in the study did not cause any signs of toxicity at egg concentrations as high as 12,000 ng/g egg. It was therefore, not possible to quantitatively determine the toxicity of PBDEs relative to 2,3,7,8-TCDD. For comparative purposes, the polybromodibenzo-p-dioxins had lethal $dose_{50}$ (LD_{50}) values ranging from 0.122-63.7 ng/g egg (their toxicity relative to 2,3,7,8-TCDD ranged from 0.0089-2.54), polybromodibenzofurans had LD_{50} values ranging from 1.5-247 ng/g egg (their toxicity relative to 2,3,7,8-TCDD ranged from 0.002-0.25), and the non-ortho substituted PBBs had LD_{50} values ranging from 168-3,910 ng/g (their toxicity relative to 2,3,7,8-TCDD ranged from 0.00012-0.0016).

Laboratory Animal Toxicity

Acute Lethality

A limited number of LD_{50} values are available for PBDEs. An intraperitoneal LD_{50} of 125 milligrams per kilogram (mg/kg) Di-BDE was reported for mice. Rat oral LD_{50}s of 5,800 and 7,400 mg/kg were reported for commercial Penta-BDE in Wistar rats. An oral rat LD_{50} value of > 5 grams per kilogram (g/kg) was reported for Octa-BDE and Deca-BDE (WHO, 1994).

Liver and Kidney Effects

Male and female Sprague-Dawley rats were administered 2.5, 25, and 250 mg/kg-day Bromkal 70-5 DE via gavages for 28 days (Fattore et al., 2001). Dose-related increases in liver and kidney weights occurred, but the increases were only significant at the highest dose. Dose-related increases also occurred with liver pathology and liver enzymes. An increase in EROD activity and a decrease in hepatic vitamin A levels were significant for males and females at the mid-dose and high-dose levels, whereas the increase in pentoxyresorufin-o-deethylase activity was significant for males and females only at the highest dose.

Male Sprague-Dawley rats were administered commercial Penta-BDE via gavages at doses of 0.44, 0.88, 1.77, 3.53, 7.06, and 14.12 mg/kg-day (Carlson, 1980). Liver enzyme induction occurred at all doses. No histological liver abnormalities were observed in the lower three dose groups. The higher dose groups were not examined histologically. A no-observed-adverse-effect-level (NOAEL) of 1.77 mg/kg-day, with an uncertainty factor (UF) of 1000, was used by the U.S. EPA to derive a reference dose (RfD) of 0.002 mg/kg-day (EPA, 2003a).

Female Sprague-Dawley rats were administered commercial Penta-BDE via the feed at doses of 2, 10, or 100 mg/kg-day (ATSDR, 2004). Hypertrophy and slight necrosis occurred in the livers of animals dosed with 2 mg/kg-day, whereas, thyroxine (T_4) was reduced at higher levels. The ATSDR (2002) considered 2 mg/kg-day to be a LOAEL with minimal effects.

Male Sprague-Dawley rats were administered technical Octa-BDE (primarily Hexa- through Nona-BDE) via gavages at doses of 0.62, 1.25, 2.51, 5.01, 10.02, or 20.04 mg/kg-day (Carlson, 1980). Liver enzyme induction occurred at all doses. No histological liver abnormalities were observed in the lower three dose groups. The higher dose groups were not examined histologically. A NOAEL of 2.51 mg/kg-day, with an UF of 1000, was used by the U.S. EPA to derive an RfD of 0.003 mg/kg-day (EPA, 2003b).

Sprague-Dawley rats were exposed via the diet to 0.01, 0.1, and 1.0 mg Deca-BDE/kg body weight for two years (Kociba et al., 1975). No effects were found on hematology, clinical chemistry, food consumption, organ weight, body weight, and incidence of histopathological lesions. A NOAEL of 1.0 mg/kg-day, with an UF of 100, was used by the U.S. EPA to derive an RfD of 0.01 mg/kg-day (EPA, 2003c).

Male Sprague-Dawley rats were exposed via the diet to 0.01, 0.1, or 1.0% commercial Octa-BDE or Deca-BDE (equivalent to 8, 80, or 800 mg/kg-day) for 30 days (Norris et al., 1975). Histopathological examination of organs revealed liver and kidney lesions and thyroid hyperplasia at all doses of Octa-BDE. Liver and kidney lesions and thyroid hyperplasia were observed at the two higher doses of Deca-BDE. The NOAEL for Deca-BDE was 8 mg/kg-day. A NOAEL was not found for Octa-BDE.

Thyroid and Neurodevelopmental Effects

The effects observed on thyroid hormone function and neurodevelopment are summarized in Table 2. Studies for these effects have included commercial mixtures, predominant congeners found in human tissues (BDE-47, 99, and 153 congeners), and one study on the Deca-BDE congener.

Table 2: Observed Effects of Exposure to PBDEs Related to Thyroid Hormone Status and/or Neurodevelopment

PBDE	Effect	Species	NOAEL	LOAEL	Study
DE-71 mixture of predominantly 45-58% Penta + 25-35% Tetra	Decrease in T_4 levels	Rat-offspring/dams	1 mg/kg-day GD6-PND21/10 mg/kg-day	10 mg/kg-day GD6-PND21/30 mg/kg-day	Zhou et al., 2002
DE-71 mixture of predominantly 45-58% Penta + 25-35% Tetra	Decrease in T_4 levels	Rat-28 day female	10 mg/kg-day for 4 days	30 mg/kg-day for 4 days	Zhou et al., 2001
DE-71 mixture of predominantly 45-58% Penta + 25-35% Tetra	Decrease in T_4 levels	Rat-female	3 mg/kg-day PND 21-26	30 mg/kg-day PND 21-26	Stoker et al., 2004
DE-71 mixture of predominantly 45-58% Penta + 25-35% Tetra	Decrease in T_4 levels	Rat-male		3 mg/kg-day PND 23-53	Stoker et al., 2004
DE-71 mixture of predominantly 45-58% Penta + 25-35% Tetra	Decrease in T_3 levels, increased TSH, induction of UDGPT	Rat-male	3 mg/kg-day PND 21-26	30 mg/kg-day PND 23-53	Stoker et al., 2004
DE-79 mixture of predominantly 31% Octa- + 45% Hepta-BDE	Decrease in T_4 levels	Rat-28 day female	3 mg/kg-day for 4 days	10 mg/kg-day for 4 days	Zhou et al., 2001
Bromkal 70-5 DE mixture almost exclusively Tetra- and Penta-BDE	Decrease in T_4 levels, LSI	Rats and mice 7 weeks female		18 mg/kg for 14 days	Hallgren et al., 2001
BDE-47 (Tetra-BDE)	Decrease in T_4 levels, LSI	Rats and mice 7 weeks female		18 mg/kg for 14 days	Hallgren et al., 2001
Saytex 111 mixture predominantly Octa	Slight fetal toxicity, preterm delivery and abortion (not reported as effect)	Rabbit	5 mg/kg-day Reported by Authors	15 mg/kg-day	Breslin et al., 1989
DE-71 mixture of predominantly 45-58% Penta + 25-35% Tetra	Preputial separation	Rat-male	3 mg/kg-day PND 23-53	30 mg/kg-day PND 23-53	Stoker et al., 2004
DE-71 mixture of predominantly 45-58% Penta + 25-35% Tetra	Reduced seminal vesicle and ventral prostate weight Delayed vaginal opening	Rat-male Rat-female	30 mg/kg-day PND 23-53	60 mg/kg-day PND 23-53	Stoker et al., 2004
BDE-47 (Tetra-BDE)	Activity profile (spontaneous locomotion) 2 and 4 months old	Mouse-male	0.7 mg/kg single dose PND 10	10.5 mg/kg single dose PND 10	Eriksson et al., 2001
BDE-47 (Tetra-BDE)	Increased locomotor activity (open field PND 80, and basal counts and duration PND 35)	Rat-male and female	0.14 mg/kg single dose on GD 6	0.7 mg/kg single dose on GD 6	Kuriyama et al., 2005

Table 2: Observed Effects of Exposure to PBDEs Related to Thyroid Hormone Status and/or Neurodevelopment (Continued)

PBDE	Effect	Species	NOAEL	LOAEL	Study
BDE-99 (Penta-BDE)	Decreased viability – litter size	Mouse	0.6 mg/kg-day GD 6 through PND 21	6 mg/kg-day GD 6 through PND 21 (30 mg/kg-day – decrease not significant)	Branchi et al., 2002
BDE-99 (Penta-BDE)	Delayed ability to climb vertical screen (2-day)	Mouse-male and female	6 mg/kg-day GD 6 through PND 21	30 mg/kg-day GD 6 through PND 21	Branchi et al., 2002
BDE-99 (Penta-BDE)	Activity profile at PND34 - 120 but not sig. at PND 22	Mouse-male and female	0.6 mg/kg-day for hyperactivity GD 6 through PND 21	0.6 mg/kg-day for rearing 6 mg/kg-day for hyperactivity GD 6 through PND 21	Branchi et al., 2002
BDE-99 (Penta-BDE)	Activity profile (spontaneous locomotion) 2 and 4 months old	Mouse-male		0.8 mg/kg single dose PND 10	Eriksson et al., 2001
BDE-99 (Penta-BDE)	Activity profile (spontaneous locomotion) 4 months old	Mouse-male		8 mg/kg single dose PND 3 and PND 10	Eriksson et al., 2002
BDE-99 (Penta-BDE)	Activity profile (spontaneous locomotion) 2 months old with and without nicotine	Mouse-male		8 mg/kg single dose PND 10	Viberg et al., 2002
BDE-99 (Penta-BDE)	Activity profile (spontaneous locomotion) 2, 5, and 8 months old	Mouse (C57/Bl)-male & female	0.4 mg/kg single dose PND 10	0.8 mg/kg single dose PND 10	Viberg et al., 2004a
BDE-99 (Penta-BDE)	Perseveration – Morris Water Maze – decrease in acquisition after change in platform location	Mouse-male		12 mg/kg single dose PND 10 lower dose animals not tested	Eriksson et al., 2001
BDE-99 (Penta-BDE)	Delayed eruption of incisors	Rat-male & female	0.06 mg/kg single dose on GD 6	0.3 mg/kg single dose on GD 6	Kuriyama et al., 2005
BDE-99 (Penta-BDE)	Delayed development of cliff-drop aversion	Rat-male	0.06 mg/kg single dose on GD 6	0.3 mg/kg single dose on GD 6	Kuriyama et al., 2005

Table 2: Observed Effects of Exposure to PBDEs Related to Thyroid Hormone Status and/or Neurodevelopment
(Continued)

PBDE	Effect	Species	NOAEL	LOAEL	Study
BDE-99 (Penta-BDE)	Increased locomotor activity (counts and duration) PND36	Rat-male and female	0.06 mg/kg single dose on GD 6	0.3 mg/kg single dose on GD 6	Kuriyama et al., 2005
BDE-99 (Penta-BDE)	Increased locomotor activity (counts and duration) PND71	Rat-male and female		0.06 mg/kg single dose on GD 6	Kuriyama et al., 2005
BDE-99 (Penta-BDE)	Decreased daily sperm production, number of sperm and spermatids, epididymis % weight	Rat-male		0.06 mg/kg single dose on GD 6	Kuriyama et al., 2005
BDE-99 (Penta-BDE)	Decreased testis weight (% bw), decrease in ejaculations	Rat-male	0.06 mg/kg single dose on GD 6	0.3 mg/kg single dose on GD 6	Kuriyama et al., 2005
BDE-153 (Hexa-BDE)	Activity profile (spontaneous locomotion) 2, 4, and 6 months old	Mouse-male	0.45 mg/kg-day single dose PND 10	0.9 mg/kg single dose PND 10	Viberg et al., 2003a
BDE-153 (Hexa-BDE)	Morris Water Maze	Mouse-male	0.45 mg/kg single dose PND 10	0.9 mg/kg single dose PND 10	Viberg et al., 2003b
BDE-153 (Hexa-BDE)	Decrease in number of hippocampal nicotinic receptors	Mouse-male		9 mg/kg single dose PND 10	Viberg et al., 2003b
BDE-203 (Octa-BDE)	Activity profile (spontaneous locomotion) 2 months old	Mouse-male		16.8 mg/kg single dose PND 3 and PND 10	Eriksson et al., 2004a
BDE-203 (Octa-BDE)	Morris Water Maze	Mouse-male		16.8 mg/kg single dose PND 3 and PND 10	Eriksson et al., 2004a
BDE-206 (Nona-BDE)	Activity profile (spontaneous locomotion) 2 months old	Mouse-male		18.5 mg/kg single dose PND 3 and PND 10	Eriksson et al., 2004a
BDE-206 (Nona-BDE)	Morris Water Maze	Mouse-male		18.5 mg/kg single dose PND 3 and PND 10	Eriksson et al., 2004a
BDE-209 (Deca-BDE)	Activity profile (spontaneous locomotion) 2, 4, and 6 months old	Mouse-male	2.22 mg/kg single dose PND 3	20.1 mg/kg single dose PND 3	Viberg et al., 2003a
BDE-209 (Deca-BDE)	Activity profile (spontaneous locomotion) 2 months old	Rat-male		6.7 mg/kg single dose PND 3	Viberg et al., 2007
BDE-209 (Deca-BDE)	Palpebral reflex, forelimb grip, struggling behavior, spontaneous locomotion, T_4 levels	Mouse-male	6 mg/kg/day PND 2-15	20 mg/kg/day PND 2-15	Rice et al., 2007

PBDEs have been shown to alter thyroid hormone levels. T_4 levels were reduced by several Tetra- through Octa-BDE mixtures in rats (Hallgren and Darnerud, 2002; Zhou et al., 2001; Zhou et al., 2002). No effect on T_4 levels was observed using a commercial mixture that is 98% Deca-BDE with doses as high as 100 mg/kg-day for four days; T_4 levels were measured on day five (Zhou et al., 2001). However, T_4 levels demonstrated a significant dose dependent decrease in mice on postnatal day 21 after six and 20 mg/kg/day on postnatal days 2-15 (Rice et al., 2007). Lower brominated single congener PBDE has also been demonstrated to reduce serum T_4 in female weanling rats (Zhou et al., 2001). Effects on T_4 levels appear to be more sensitive to perinatal exposure than weanling or adult exposure as demonstrated by a predominantly Tetra- and Penta-BDE mixture (Zhou et al., 2002). Triiodothyronine (T_3) levels did not appear to be affected in most studies and were only slightly decreased at higher doses (Zhou et al., 2001; Stoker et al., 2004). Minimal alterations in thyroid stimulating hormone (TSH) levels have been observed at higher exposures only (Stoker et al., 2004). These studies indicate that clinical measurements of the pituitary-thyroid axis are not observed after PBDE exposure, although serum T_4 levels may be significantly reduced. The decrease in circulating T_4 levels may be partially related to increased metabolism of T_4 through PBDE induction of T_4 metabolizing enzymes including urinediphosphate-glucuronosyltransferase (UDPGT). These changes result in biliary excretion of metabolized T_4 (Hallgren and Darnerud, 2002; Zhou et al., 2001). However, T_4 reductions occur at PBDE doses lower than those required for UDPGT induction, indicating this may not be a significant mechanism for T_4 reduction. In vitro assays indicate that hydroxylated PBDEs bind the T_4 serum transporting protein transthyretin (deWit, 2002; Hallgren and Darnerud, 2002; Hallgren et al., 2001; Zhou et al., 2001; Zhou et al., 2002), which could also lead to decreases in serum T_4 levels. These and other mechanisms may be involved in PBDE-related alterations in T_4 levels.

Although many of these PBDE-related effects on T_4 levels have been demonstrated in laboratory animals, it is not known if these same effects could occur in humans. It has been long understood that iodine insufficiency and/or hypothyroidism during pregnancy can cause profound effects on the developing fetus leading to a syndrome called Cretinism. This syndrome generally includes impaired growth and development of the brain, frequently resulting in dwarfism and mental retardation. Although generally used clinical measurements may not demonstrate hypothyroidism from PBDE exposure in animals, irreversible effects on fetal brain development may result from the reduced T_4 levels observed from PBDE exposures. Morreale de Escobar et al., (2000), determined that hypothyroxemia without “clinical hypothyroidism” (as measured by a decrease in T_3 or increase in TSH) may result in significant effects on the developing brain of human fetuses. Although other fetal tissues appear to be more affected by low T_3 levels, reduced T_4 levels appear to adversely impact the developing brain even when T_3 levels are normal. It appears that fetal brain tissue has enzymes that convert maternal T_4 to T_3, and that these enzymes have not been observed in other fetal tissues. In addition, prior to the onset of fetal thyroid function, T_3 levels found in normal developing fetal brain are much higher than the very low circulating fetal T_3 levels found early in gestation. Maternal T_4 levels early in gestation appear to be critical in normal neurodevelopment. Infants with congenital hypothyroidism (CH), when maternal thyroid function is normal, can be effectively treated after birth. However, infants with CH whose mothers had hypothyroxemia have permanent neurodevelopment impairment even with postnatal treatment that prevents other cretinistic effects, e.g., skeletal and muscular (Morreale de Escobar et al., 2000). Pop et al., (1999), demonstrated that even in healthy women without hypothyroidism or other complicating factors, psychomotor development was significantly impaired with low fetal T_4 levels at 12 weeks of gestation (prior to the onset of fetal thyroid function), but not at 32 weeks of gestation. A trend for decreased mental development with decreased fetal T_4 levels at 12 weeks was also noted,

although not significant in this study. Morreal de Escobar et al., (2000) and Pop et al., (1999), recommend prenatal screening for thyroid hormone measurements to include those that would identify hypothyroxemia, as well as "clinical hypothyroidism."

Some PBDEs have also been demonstrated to alter cognitive and behavioral functions in mice after perinatal exposure. Alterations in locomotor activity have been demonstrated in male and female mice with perinatal exposures to BDE-47, 99, 153, 203, 206, and 209. The most profound effect is a decrease in habituation that becomes more pronounced with age (Branchi et al., 2002; Eriksson et al., 2001; Eriksson et al., Viberg et al., 2004). The critical exposure period for this effect in mice appears to be around postnatal day (PND) 10 for BDE-47, 99, 153, 203, and 206 (Eriksson et al., 2002, Viberg et al., 2004, Eriksson et al., 2004a).

The alteration in locomotor activity pattern has also been observed with Deca-BDE (Deca-BDE) (Viberg et al., 2003a; Viberg et al., 2007; Rice et al., 2007). All three studies demonstrated significant alterations in activity patterns at 20-20.1 mg/kg postnatal dosing in males. In rats, Viberg et al., (2007), saw significant changes in locomotor activity at doses on PND 3 of 6.7 and 20.1 mg/kg. Rice et al. also observed significant changes in palpebral reflex, forelimb grip, struggling behavior and T_4 levels in mice at 20 mg/kg. Viberg et al., (2003a) found that the alteration in locomotor activity pattern occurred only after exposure on PND 3 and not PND 10 as observed with other PBDEs and PCBs (Viberg et al., 2003a). This study also evaluated ^{14}C-labeled Deca-BDE uptake in several tissues. Although other tissues showed decreased uptake between 24 hours post-exposure and seven days post-exposure, the brain uptake levels were significantly increased at day seven. The authors (Viberg et al., 2003a) speculate this may be due to metabolism of the Deca-BDE into a lower brominated PBDE prior to causing the neurodevelopmental effects. A subsequent study demonstrated that Octa- and Nona-congeners (BDE-203 and 206, respectively), potential metabolites of Deca-BDE, also produce the same alterations in locomotor activity patterns after exposure on PND 10 (Eriksson et al., 2004a). Interestingly, BDE-203 also demonstrated the same alteration in activity patterns after exposure on PND 3.

Similar alterations in locomotor activity have also been observed in rats after a single dose prenatal exposure, gestation day (GD) 6, to BDE-47 and 99 (Kuriyama et al., 2004; Kuriyama et al., 2005). As with the mice, the alterations were more severe for some effects, as the animals matured.

Alterations in other cognitive behaviors after perinatal exposure to PBDEs include: 1) early life deficits, as observed by a two-day lag in the development of screen climbing ability from perinatal exposure to BDE-99 in mice (Branchi et al., 2002) and rats (Kuriyama et al., 2005); 2) deficits in spatial learning in adult animals as demonstrated by increased latency to find a swim platform. The effect was more pronounced for the relearn trials after the platform was moved following exposure to BDE-99, 153, 203 or 206 on PND 10 (Eriksson et al., 2001; Viberg et al., 2003b; Eriksson et al., 2004a). In addition, decreases in mouse hippocampal nicotinic receptors (Viberg et al., 2003b), and increased release of arachidonic acid from rat cerebellar granule neurons (Kodavanti and Derr-Yellin, 2002) have been observed after PBDE exposure.

Other fetal effects reported to be associated with PBDE exposure include: 1) delayed ossification of the sternabrae in rabbits at maternally toxic doses of the Octa-BDE product, Saytex 111 (Breslin et al., 1989); 2) delayed eruption of incisors in male and female rats after exposure to BDE-99 on GD 6 (Kuriyama et al., 2005), 3) alterations in reproductive organs and function after postnatal exposure to the Penta-BDE product DE-71 (Stoker et al., 2004), and prenatal exposure to BDE-99 (Kuriyama et al., 2005). Although not evaluated, Breslin et al.,

(1989), reported that two litters were delivered prior to normal term, and another aborted the litter at the high dose (15 mg/kg-day). Branchi et al., (2002), reported a decrease in litter size that was significant at the middle dose (6 mg/kg-day), but not at the high dose (30 mg/kg-day).

Some of the neurodevelopmental effects observed with PBDE perinatal administration may be secondary to decreases in T_4 levels (deWit, 2002; Branchi et al., 2003). Similar alterations in locomotor activity and spatial learning abilities have been observed following perinatal treatments to reduce T_4 levels (Branchi et al., 2003; Goldey et al., 1995). Unfortunately, most thyroid hormone studies have used rats, and most neurodevelopmental studies have used mice to evaluate effects of PBDEs. The very limited data on neurodevelopmental effects in rats suggest that some of these effects occur at lower doses than those observed to decrease T_4 levels. Rice et al., (2007), observed a dose dependent decrease in T_4 levels and alterations in reflexes and locomotion in the same male mice. There was not a significant change in T_4 levels or these behaviors in female mice in this study. Therefore, evaluation of whether the effects on the developing brain from PBDEs is through direct or indirect e.g., thyroid mechanisms, is not clear at this time. Future studies should consider evaluation of auditory thresholds. Goldey et al., (1995), demonstrated in rats that decreased perinatal T_4 level results in auditory threshold deficits; this effect appears to be more sensitive in rats than alterations in motor activity. Another critical consideration is that the hypothyroxemia and some of the altered neurological and neurobehavioral effects are similar to those observed after exposures to noncoplanar PCBs. Eriksson et al., (2006), evaluated the potential additive effects of BDE-99 and PCB-52. They found a greater than additive effect of the two chemicals combined on alteration of spontaneous locomotor behavior and habituation capability in mice dosed on PND 10. Further evaluation of potential additivity of effects from these two classes of chemicals should be considered.

Mutagenicity

Limited data are available on the mutagenicity of PBDEs. According to the National Toxicology Program (NTP, 1986), Deca-BDE was not mutagenic in *Salmonella Typhimurium* strains (TA1535, TA1537, TA 98, or TA100) or in the mouse lymphoma L5178Y/$TK^{+/-}$ assay with or without enzyme induction. This compound also did not cause chromosomal aberrations or sister-chromatid exchanges with or without enzyme induction. Norris et al., (1975) found no cytogenic effects in the bone marrow cells of rats exposed to a Deca-BDE mixture (77.4% Deca-BDE, 21.8% Nona-BDE, and 0.8% Octa-BDE) in a one generation reproduction study. Exposure of Chinese hamster cells to BDE-47, BDE-12, or BDE-1 caused increased gene recombination at the Hypoxanthine-guanine Phosphoribosyltransferase locus (Helleday et al., 1999). A study in rats and mice found that Tetra-BDE was covalently bound to macromolecules in various tissues with evidence of a reactive epoxide intermediate (Orn et al., 1998). The congener BDE-99, 5-Penta-BDE was not mutagenic in *Salmonella Typhimurium* or *Escherischia Coli*, and it was not clastogenic in *Allium Cepa* (Evandri et al., 2003).

Carcinogenicity

Deca-BDE is the only PBDE that has been tested for carcinogenicity. A dietary study by NTP (1986) found some evidence of carcinogenicity for male and female F344/N rats as shown by increased incidences of neoplastic nodules of the liver in low dose (25,000 parts per million [ppm]) males and high dose (50,000 ppm) males and females. There was equivocal evidence of carcinogenicity for male B6C3F1 mice as shown by increased incidences of hepatocellular tumors in the low dose group and of thyroid gland follicular cell tumors in both dose groups.

There was no evidence of carcinogenicity for female B6C3F1 mice receiving 25,000 or 50,000 ppm Deca-BDE in the diet.

There are a few things to consider when assessing the carcinogenicity potential of Deca-BDE. For instance, the NTP (1986) study used high doses, Deca-BDE was poorly absorbed, and the study used a technical grade product i.e., 95-97% pure Deca-BDE, which contained impurities. An earlier bioassay in rats (Kociba et al., 1975), used fewer animals and much lower doses, and found no significant increase in the incidence of tumors. Based on this information, McDonald (2002), considered the carcinogenicity concern over Deca-BDE to be low.

The other PBDE congeners have not been tested for carcinogenicity. Congeners other than Deca-BDE would be more of a concern with respect to carcinogenicity, since they would be more readily absorbed and more slowly eliminated. In addition, several congeners i.e., Tetra-, Penta-, and Octa-BDE, have been shown to exhibit a greater potential for thyroid disruption and enzyme induction than Deca-BDE. Lastly, some of the other PBDE congeners have tested positive in some mutagenicity tests (McDonald, 2002).

Wildlife Toxicity

Aquatic Life Toxicity

Several studies have examined the potential for PBDEs to cause reproductive or developmental effects in aquatic life. An approximate no observable effect concentration of 5 µg/L was found for a Tetra- to Hexa-BDE mixture in a 21-day life cycle test in daphnids (Darnerud, 2003). Holm et al., (1993), exposed female sticklebacks to two dietary concentrations of Bromkal 70-5 for three and one-half months. Neither concentration affected the number of eggs laid, but the highest exposure caused a reduction in spawning success. Hornung et al., (1996), found no effects on fish eggs injected with either BDE-47; BDE-85; or BDE-99 at concentrations up to 12 ug/g egg. Five-day effective median concentrations for the inhibition of larval development in a marine copepod (*Acartia tonsa*) of 12.8, 12.5, 4.2 and 1.2 µg/L were found for BDE-28, BDE-47, BDE-99, and BDE-100, respectively (Wollenberger et al., 2005).

Exposure of aquatic life to PBDEs has also been shown to cause changes in a variety of blood parameters. Tjarnlund et al., (1998), found a reduction in glutathione reductase, hematocrit, and blood glucose levels in rainbow trout exposed to dietary concentrations of BDE-47 or BDE-99. Kierkegaard et al., (1999), found enlarged livers, increased lactate concentrations, and decreased lymphocytes in rainbow trout administered doses of 7.5 to 10 mg Deca-BDE/kg-day for 120 days. Juvenile lake trout exposed to a mixture of 13 PBDE congeners (2.5 or 25 ng/g per PBDE congener) via their diet for 56 days, exhibited a decrease in plasma thyroxine levels, but no effects were observed on triiodothyronine levels (Tomy et al., 2004). Juvenile turbots exposed to 5 µg/L BDE-47 for three weeks exhibited a decrease in plasma triiodothyronine levels, but no effects were observed on the concentrations of testosterone, estradiol, or thyroxine (Jenssen et al., 2004).

Two studies have also examined the potential for PBDE to cause mortality in aquatic life. A 48-hour LC_{50} (lethal concentration to 50% of the exposed group) of 0.36 mg/L and a 96-hour LC_{50} of 4.94 mg/L were found for daphnids and bluegill sunfish, respectively exposed to Mono-BDE (WHO, 1994). Wollenberger et al., (2005), found 48-hour LC_{50}s of 108, 2370, 705 and 520 µg/L for a marine copepod (*Acartia tonsa*) exposed to BDE-28, BDE-47, BDE-99, and BDE-100, respectively.

Other Wildlife

A positive correlation was found between the concentration of PBDEs in the blubber of grey seals during their first year of life and the concentrations of triiodothyronine and thyroxine in their blood (Hall et al., 2003). However, It could not be determined whether these effects were due to PBDEs, since the study did not determine whether the same correlation existed for other contaminants. No studies were found in the literature which examined the effects of PBDEs on mammalian wildlife.

Several laboratory studies have examined the toxicity of PBDEs to kestrels (Fernie et al., 2005a, 2005b, 2006). In these studies, kestrel eggs were injected with a PBDE mixture consisting of BDE-47, BDE-99, BDE-100, and BDE-153, at approximately 19 days of incubation. The total concentration of PBDEs injected into the egg (18.7 ug PBDEs) and the congener profile were similar to those found in herring gull eggs from the Great Lakes basin. The birds were also dosed via gavage with the same mixture from the first day of hatching through day 29. The concentration of PBDEs administered via gavages (15.6 ng/g body weight/d) approximated the amount measured in lake trout. PBDE-exposed birds were larger, gained weight more quickly, and ate more food. No effects were found on hatching or fledging success (Fernie et al., 2006). The birds also had lower plasma thyroxine, plasma retinol, hepatic retinol, and retinyl palmitate concentrations than control birds. Hepatic oxidative stress was also induced in treated birds (Fernie et al., 2005a). Finally, the treated kestrels had greater T-cell mediated immunity and exhibited structural changes in the spleen, bursa, and thymus (Fernie et al., 2005B).

TOXICOKINETICS

Mammalian Toxicokinetics

This section relies very heavily on three review articles (deWit, 2002; Hakk and Letcher, 2003; Birnbaum and Staskal, 2004). Toxicokinetics is an important factor when evaluating the exposure to environmental contaminants. The process by which chemicals enter the body (absorption), the levels in different organs and tissues (distribution), breakdown into other chemicals (metabolism), and the ability of the body to eliminate the chemical or its metabolites (elimination/excretion) can help determine the bioaccumulation, fate, and toxicity of contaminants. Analyses of human and wildlife tissues show that some of the PBDEs are bioaccumulative. A brief summary of the limited experimental data on the toxicokinetics of PBDEs follows.

Absorption

Generally, the literature demonstrates that the lower brominated PBDEs are readily absorbed (>50%) after oral exposure with absorption decreasing as the level of bromination increases. Deca-BDE appears to be less well absorbed. Although recent studies indicate there can be 10-65% absorption of Deca-BDE after oral exposure (Sandholm et al., 2003; Birnbaum and Staskal, 2004).

Male Sprague-Dawley rats were administered Bromkal 70 (mostly BDE-47 and 99) or DE-79 (mostly Hexa- through Nona-BDE congeners) in the feed for 21 days at 33 mg/day/rat. In general, there were no absorption differences for the lower brominated Bromkal 70 congeners, i.e., the tissue congener distribution patterns resembled that of the commercial mixture. However, a decrease in bioavailability was observed with increasing bromination with DE-79 (Hakk and Letcher, 2003).

Studies have shown that Tetra and Penta congeners, BDE-47, BDE-99, and BDE-100, are readily absorbed by male rats (Hakk and Letcher, 2003; Hakk et al., 2006). A recent study of BDE-47 in female mice demonstrated that this Tetra congener is readily absorbed through inhalation and oral routes (>80%), with less (~62%) dermal absorption (Staskal et al., 2005). Another recent study had similar results for oral absorption for BDE-47 (85%) in mice with slightly less absorption (75%) observed for rats (Sanders et al., 2006).

There is some apparent conflict regarding the oral bioavailability of Deca-BDE. Previous studies indicated very poor gastrointestinal absorption. Also reported was very little tissue uptake of ^{14}C labeled Deca-BDE, with the only significant levels measured in adipose tissues. More recent studies have demonstrated greater than 10-65% absorption of the administered Deca-BDE doses (Morck et al., 2003; Sandholm et al., 2003; Viberg et al., 2003b; Birnbaum and Staskal, 2004). Sandholm et al., (2003), demonstrated at least 26% oral absorption with suggestive evidence from phenolic metabolites (65% metabolites in feces) that greater

absorption had occurred with first pass metabolism and elimination of metabolites through bile into the feces. It is also possible that intestinal flora is responsible for metabolite formation (Sandholm et al., 2003).

Distribution

Generally, the lower brominated BDEs appear to be distributed predominantly to lipid-rich tissues within a few days of administration, with the greatest concentrations found in adipose tissue. The tissue concentration differences are not as extreme on a lipid basis as on a wet weight basis. Deca-BDE appears to be distributed more to highly perfused tissues such as the liver and the heart.

Approximately 87% of the BDE-47 remained in the tissue at five days in rats; the highest concentration was deposited in the adipose tissue, followed by lung, then liver and kidney, with smaller amounts deposited in the brain. Only parent compound was found in adipose tissue, kidney, and brain. However, trace amounts of OH-metabolites were detected in the liver and lung (Hakk and Letcher, 2003). Staskal et al., (2005), demonstrated that tissue distribution trends were similar across the intravenous, oral, inhalation and dermal routes in female mice. The highest tissue concentrations were in adipose and liver. Concentrations of BDE-47 peaked at three hours for blood, kidney, liver, and lung, at eight hours for brain and muscle, and 1-3 days for adipose and skin tissues.

After 72 hours, BDE-99 was distributed to lipophilic tissues such as adipose tissue, skin, and gastrointestinal tract of rats (Hakk and Letcher, 2003).

^{14}C-labeled Tetra- and Penta-BDE congeners were found in liver, fat, adrenal, ovary, lung, and brain (shortly after administration) of pregnant mice with low fetal uptake. Tissue levels dropped after administration with radioactivity remaining in fat deposits. Lactational exposure of the Penta-congeners was substantial with neonate plasma levels more than two times the maternal plasma levels (deWit, 2002).

The highest concentrations of Deca-BDE were found in the plasma and highly perfused tissues after oral administration. Mouse brain, heart, and liver uptake levels of ^{14}C labeled Deca-BDE varied depending on the age of the animals (PND 3, 10, or 19) with greater uptake and retention during PND 3 and PND 10, as compared to PND 19 (Viberg et al., 2003a).

Metabolism

Generally, PBDEs appear to undergo some metabolism, with the higher brominated congeners (especially Deca-BDE) more readily metabolized. There also appear to be species differences in metabolism with mice appearing to more readily metabolize some congeners than rats.

The information about PBDE uptake, enzyme induction, elimination, and metabolism is largely restricted to *in vitro* and *in vivo* experiments in rodents.

Most of the congener-specific PBDE metabolism studies in the rat and mouse have been done with BDE-47, BDE-99, and Deca-BDE. One study showed that although BDE-47 was readily absorbed by male rats, metabolism was slow (only 14% and <0.5% of the dose was excreted in the feces and urine by five days, respectively). The major compound found in rat feces was parent compound (>85%) (deWit, 2002; Hakk and Letcher, 2003).

The mouse is more capable of metabolizing BDE-47 than the rat. In one study, approximately 33% of a dose of BDE-47 was excreted in urine by five days; approximately 20% of the portion found in urine was characterized as parent compound. Over 20% of the dose was excreted in the feces in five days and most was the metabolite fraction (the same six metabolites characterized in the rat feces). Almost 47% of the dose remained in the tissues at five days, with adipose tissue containing the highest concentration of BDE-47 (Hakk and Letcher, 2003).

A single, oral dose (2.2 mg/kg) of radiolabeled BDE-99 was administered to male rats (both conventional and bile duct-cannulated rats). Metabolism of BDE-99 to water-soluble metabolites was very low. The feces from conventional rats contained minor amounts of metabolites, while the remainder was parent compound. Fecal metabolites consisted of two mono-OH-Penta-BDE metabolites and two debrominated mono-OH-Tetra-BDE metabolites (Hakk and Letcher, 2003).

Rats metabolized Deca-BDE to fecal metabolites via oxidative debromination. These included debrominated mono-OH- and ortho-MeO-OH-BDEs. From a ^{14}C-Deca-BDE intravenous study, of the 74% of the administered dose found in the feces after 72 hours, 63% were metabolites and only 37% was the parent compound (deWit, 2002). Other studies demonstrated that hydroxyl/methoxy metabolites with 5-7 bromines are found in rat bile and that hydroxylated Octa- and Nona-BDEs are found as major phenolic metabolites after oral administration in rats (Birnbaum and Staskal, 2004; Sandholm et al., 2003). There is also evidence that these phenolic metabolites are retained resulting in more significant exposures to these metabolites after 3-7 days than from the parent Deca-BDE (Sandholm et al., 2003).

A human study evaluating occupational exposure to Deca-BDE demonstrated some workers with high exposures to Deca-BDE by blood levels elevated 5-100 times that of the reference workers. Among those workers with higher exposures to Deca-BDE, there were also elevated blood levels for Octa- and Nona-BDE. The elevated levels of the Octa- and Nona-compounds were a greater proportion to Deca-BDE concentrations than the trace amounts of Octa- and Nona-congeners found in the commercial Deca-BDE product used by these workers. These results are suggestive that there may be reductive debromination occurring after exposure to Deca-BDE resulting in Octa- and Nona-BDE metabolites. The authors do not rule out the possibility of preferential bioavailability and/or retention of these congeners as alternate hypotheses for these results (Thuresson et al., 2005).

Elimination

PBDEs appear to be predominantly eliminated by fecal excretion in rats. A component of this fecal content appears to be absorbed parent compound and metabolites excreted into the gut via bile. Urinary excretion appears to be a minor component for rats, but may be equally important to fecal excretion in mice. Elimination half-lives for lower brominated congeners (Tetra- through Hexa-BDEs) appear to increase with the amount of bromination. The higher brominated congeners appear to be more readily metabolized and excreted with shorter half-lives. Longer half-lives may be evident in humans as compared to rodent species (deWit, 2002).

A rat study investigating the half-lives of various constituents of Bromkal 70 (a commercial grade Penta-mixture) reported that Tetra-, Penta-, and Hexa-BDE congeners were slowly eliminated following a single oral dose. The majority of the bioaccumulation after four days occurred in the adipose tissue. Very little, if any, PBDE congeners remained in extra-adipose tissue after four days. Half-lives ranged from 19-119 days, and the half-life generally increased

with increasing bromination. These data were obtained following a large dose of 300 mg/kg (greatly in excess of the threshold for minimal cytochrome P450 induction [3-10 mg/kg]) (Hakk and Letcher, 2003).

Elimination of BDE-47 appears to be biphasic in female mice (Staskal et al., 2005). The first, more rapid phase ($t_{½}$ = 1.5 days) appears dependent on urinary excretion. The terminal phase elimination rate ($t_{½}$) for the whole body was 23 days. In this study of female mice, urinary excretion was dose dependent with a lower percentage of the dose excreted at higher doses. The majority of the urinary excretion was as parent compound suggesting an active transport mechanism in mice.

Fecal excretion was the major route of elimination of BDE-99 in rats. Seventy-two hours following oral administration of ^{14}C-BDE-99, 43% of the dose was excreted in conventional rat feces, and in the bile duct-cannulated rat feces, >86% was excreted. Although, metabolism of BDE-99 to water-soluble metabolites was very low, most of the radioactivity in the urine was due almost exclusively to metabolites (not characterized) (deWit, 2002).

Human elimination half-lives were estimated from workers for a Hepta-congener (BDE-183) and Deca-BDE. The estimated half-lives were 86 days for BDE-183 and 6.8 days for Deca-BDE (deWit, 2002; Sjodin et al., 2003b).

In summary, PBDEs appear to be adequately absorbed to accumulate in human tissues. Lower brominated congeners (Tetra- through Hexa-PBDEs) appear to be more readily absorbed and less metabolized with less subsequent excretion, therefore, tending to bioaccumulate. Deca-BDE is not as readily absorbed, and is more readily metabolized and excreted. Metabolic by-products include hydroxylated less brominated congeners. Some of these metabolites may be biologically active.

There is some evidence that some of the hydroxylated Tri- through Penta- brominated metabolites will bind transthyretin, a thyroid hormone transport protein. It is speculated that this may be one mechanism by which PBDEs decrease T_4 levels. It is not known if other potentially adverse effects are directly affected by parent PBDEs or their metabolites.

Aquatic Organism Toxicokinetics

Fish

Fish have been found to metabolize PBDEs. For example, Sinkkonen et al., (2004), observed methoxylated-PBDEs in fish of the Baltic, Atlantic, and Arctic environments, whereas, Marsh et al., (2004), reported identifying at least one hydroxylated metabolite of anthropogenic PBDEs in salmon (Salmo salar) blood.

The accumulation of PBDEs has been studied in only a few fish species. In a study using captive northern pike, the uptake efficiency of BDE-47 was determined to be 90%, while the uptake efficiencies of BDE-99 and BDE-153 were 60% and 42%, respectively (Burreau et al., 1997). Burreau et al., (2000), administered a single dose of ^{14}C-labeled BDE-47 to northern pike via their food and found an uptake efficiency of 96%. In general, BDE-47 accumulated in the most lipophilic tissues. BDE-47 was not readily metabolized to compounds that could be easily eliminated, since the concentration of the PBDE in highly lipophilic tissues did not diminish significantly with time. Holm et al., (1993), determined an uptake efficiency of 20% for the three-spined stickleback exposed to Bromkal 70-5DE via their diet.

Different fish species demonstrate different metabolic capacities (Wolkers et al., 2004). Extremely low accumulations of PBDEs were routinely observed in white suckers and common carp in comparison to rainbow trout and mountain whitefish (1-2 orders) from the same location in Washington (Johnson and Olson 2001). This difference may be due partly to dietary differences; however, the magnitude of the difference suggests a higher metabolic activity in suckers and carp.

Common carp residing close to suspected PBDE point sources contained an unusual pattern of accumulated PBDE congeners. BDE-99 was significantly depleted in tissues relative to the tissues of other fish species from the same geographical area (Dodder et al., 2002; Hale et al., 2001). Stapleton et al., (2002), studied the uptake, metabolism, and depuration of mixtures of certain PBDE congeners in common carp. Carp were exposed to a diet containing BDE-47, 99, 100, 153, 154, and 180 for 25 days. Rapid uptake of BDE-47, 100, and 154, but low uptake of BDE-99, 153, and 183 was observed (similar to the PBDE congener pattern in carp from the wild). Debromination of BDE-154 was suggested in another experiment using only BDE-183. Separate experiments with Deca-BDE showed poor uptake by carp, but debromination was suggested by the presence of several Hexa- through Octa-BDE congeners.

The possible debromination of Deca-BDE has been studied in fish. The intestinal absorption of Deca-BDE was studied in rainbow trout (Kierkegaard et al., 1999). The calculated uptake efficiency of Deca-BDE was extremely low. The study found no increase in the muscle concentration of BDE-47, 99, or 100, and no evidence for the debromination of Deca-BDE was found. However more recently, Deca-BDE was shown to debrominate in carp (Stapleton, 2003; Stapleton et al., 2004a).

Stapleton et al., (2003, 2004a), provided evidence that Deca-BDE may be debrominated in carp. In this study, young carp were exposed to Deca-BDE via their diet for 60 days followed by a 40-day depuration period. Deca-BDE did not accumulate in the fish during the experiment. However, there were seven debrominated metabolites of Deca-BDE that accumulated in whole fish and liver tissues over the exposure period including BDE-154 and BDE-155. These metabolites were identified as Penta- to Octa-BDEs. Once Deca-BDE exposure was stopped, the Penta-congeners continued to increase, further suggesting metabolism of Deca-BDE. Less than 1% of the Deca-BDE fed to the carp accumulated in the fish as the lower brominated PBDEs. Although this percentage of accumulation seems minimal and provides evidence for the limited bioavailability of Deca-BDE, it is not well understood the degree of bioaccumulation that will occur in the environment given the continued inputs.

There is also some evidence that other PBDEs can be debrominated by fish. Stapleton et al., (2004b), exposed carp to either BDE-99 or BDE-183 via their diet for 62 days followed by a 37-day depuration period. Some of the BDE-99 was debrominated to BDE-47, whereas, some of the BDE-183 was debrominated to BDE-154 and another unidentified Hexa-BDE. At least 10% of the BDE-99 mass in the gut was debrominated to BDE-47 and assimilated in the carp, whereas, approximately 17% of the BDE-183 mass was debrominated and accumulated in carp tissues.

Juvenile lake trout were exposed to a mixture of 13 PBDE congeners for 56 days followed by a 112 day depuration period (Tomy et al., 2004). Three PBDE congeners, not present in the food or in the control fish, were found in the exposed fish. The bromine substitution pattern of one of these congeners, BDE-140, suggests that it arose from the debromination of Deca-BDE. In addition, the half-lives for some congeners were different from the expected values suggesting

that some congeners were being converted to others. The researchers surmised that BDE-85, 183, 90, and 209 were the source of the debrominated PBDEs.

Other Aquatic Organisms

Blue mussels from the Baltic Sea were exposed to BDE-47, 99, and 153 for 44 days and then allowed to depurate for 26 days. This method allows for the derivation of clearance rate coefficients and bioaccumulation factors. BDE-47 and 99 had the highest uptake clearance rate coefficients, but each congener was readily absorbed (Gustafsson et al., 1999).

Grey seals (*Halichoerus grypus*) were found to exhibit, on average, high absorption (89-99%) of PBDE congeners including Deca-BDE (Thomas et al., 2005). The half-life of Deca-BDE in blood was estimated to be 8.5-13 days (Thomas et al., 2005). One month after the end of the Deca-BDE exposure, measurable concentrations were found in the blubber of the seals. Deca-BDE resided in the blood of the seals for only a few days, but remained long-term in the blubber (Thomas et al., 2005).

ENVIRONMENTAL FATE

Chemical Characteristics and Environmental Behavior

Chemical and physical properties of the commercial and technical formulations of PBDEs are presented in Table 3.

Environmental Persistence

PBDEs are expected to persist in the environment for many years with minimal degradation. Based on a modeling exercise, BDE-47, 99, and 209 were estimated to have the same soil and water half-life of 150 days and a sediment half-life of 600 days (Palm et al., 2002). Palm et al., (2002), also reported that congener half-lives in air increased with bromination. However, Wania and Dugani (2003) found that the air-water partition coefficient decreased with the increase in bromine atoms. Atmospheric fate and dynamics of PBDEs are not well understood.

PBDEs have limited mobility in the environment, which is reflected in their high affinity to bind to sediment, e.g., log K_{oc}, low water solubility, and low volatility (Watanabe and Sakai, 2003). Log K_{oc} values were found to increase with the number of bromine atoms (Watanabe and Sakai, 2003). However, this low mobility has not prevented these chemicals from being dispersed around the globe, (see section entitled, Levels in the Environment). Congener BDE-47 has been found to be appreciably lost from a surface by advection in air, suggesting the potential for long-range transport (Palm et al., 2002). Wania and Dugani (2003) reported that lower bromine-containing congeners were more likely to experience long-range transport. Furthermore, the lower brominated compounds are predicted to be more volatile and water soluble, relative to the higher brominated compounds (Watanabe and Sakai, 2003).

Bioaccumulation

Based on log K_{ow} values, PBDEs would be expected to accumulate in aquatic biota to higher concentrations than those found in water and the organism's food, i.e., significant bioaccumulation. Bioaccumulation in the environment has been well documented in numerous species and at numerous locations globally, (see section entitled, Levels in the Environment). The log K_{ow} values have been found to increase with increasing bromine atoms on the molecule (Gouin and Harner, 2003), however, chemicals with log K_{ow} values greater than eight do not tend to bioaccumulate well. Generally, the Tetra- (log K_{ow}: 5.9-6.2), Penta- (log K_{ow}: 6.6-7.0), and Hexa- (log K_{ow}: 6.8-7.9) brominated congeners tend to bioaccumulate to the greatest extent.

Degradation

Although the rate or degree of Deca-BDE bioaccumulation is not well characterized, questions exist regarding the photolytic degradation of Deca-BDE into lower bromine-containing congeners that do undergo bioaccumulation. Hua et al., (2003), determined that 12-70% of Deca-BDE is phototransformed to lower brominated congeners, although the lower congeners were not quantified. The degree of phototransformation varied with the substrate to which the chemical was bound and the amount of applied light. Reagent grade water solutions resulted in 70% degradation in 72 hours. Humic acid solutions reduced the degradation to 30% in the same time period (72 hours). Humic acid-coated sand particles had the lowest degradation (12%) after 96 hours of exposure.

Table 3: Physical and Chemical Properties of PBDE Technical Formulations (ATSDR, 2004)

Property	Penta-Formulation	Octa-Formulation	Deca-Formulation
Chemical Formula	$C_{12}H_5Br_5O$	$C_{12}H_2Br_8O$	$C_{12}Br_{10}O$
CAS Number	32534-81-9	32536-52-0	1163-19-5
Molecular Weight	564.75[a]	801.47[a]	959.22[a]
Color	Clear, amber to pale yellow	Off-white	Off-white
Physical State	Highly viscous liquid	Powder	Powder
Melting Point	-7 to -3 ^oC (commercial)	85-89 ^oC (commercial); 200 ^oC (range 167– 257); 79-87 ^oC; 170-220 ^oC	290 – 306 ^oC
Boiling Point	>300 ^oC (decomposes >200 ^oC)	Decomposes >300 ^oC (commercial)	Decomposes >320, >400, and at 425 ^oC
Density (g/mL)	2.28 at 25 ^oC; 2.25–2.28	2.76, 2.8 (commercial)	3.0, 3.25
Odor	No Data	Faint	Odorless
Water Solubility	13.3 μg/L (commercial); 2.4μg/L (pentabromodiphenyl ether component); 10.9 μg/L (Tetrabromodiphenyl ether component)	< 1 ppb at 25 ^oC (commercial); 1.98 μg/L (Heptabromodiphenyl ether component)	< 0.1 μg/L
Organic Solvent(s) Solubility	10 g/kg Methanol; miscible in Toluene	Acetone (20g/L); Benzene (200 g/L); Methanol (2 g/L) all at 25 ^oC	Acetone (0.05%); Benzene (0.48%); Methylene bromide (0.42%); Xylene (0.87%); Toluene (0.2%)
Log K_{ow}	6.64-6.97; 6.57 (commercial)	6.29 (commercial)	6.265
Log K_{oc}	4.89-5.10	5.92-6.22	6.80
Vapor Pressure	$2.2x10^{-7}$ – $5.5x10^{-7}$ mmHg at 25 ^oC; $3.5x10^{-7}$ mmHg (commercial)	$9.0x10^{-10}$ – $1.7x10^{-9}$ mmHg at 25 ^oC; $4.9x10^{-8}$ mmHg at 21 ^oC (commercial)	$3.2x10^{-8}$ mmHg; $3.47x10^{-8}$ mmHg
Henry's Law Constant (atm-m^3/mole)	$1.2x10^{-5}$; $1.2x10^{-6}$; $3.5x10^{-6}$	$7.5x10^{-8}$; $2.6x10^{-7}$	$1.62x10^{-6}$; $1.93x10^{-8}$; $1.2x10^{-8}$; $4.4x10^{-8}$
Autoignition Temperature	Decomposes >200 ^oC	Decomposes >330 ^oC (commercial)	Not Applicable
Flammability Limits	Not Applicable (flame retardant)	Not Applicable (flame retardant)	Non-flammable
Conversion Factors	1 ppm = 23.48 mg/m^3 at 20 ^oC	No Data	No Data

[a]OECD Environmental Monograph No. 102 (1995)

Soderstrom et al., (2004), found that Deca-BDE debrominated to Nona- through Tetra-congeners under artificial ultraviolet light and under natural outdoor conditions. Regardless of

the matrices into which Deca-BDE was placed, a similar degradation pattern of BDE congeners was observed (Soderstrom et al., 2004; Eriksson et al., 2004b). Similar to Hua et al., (2003), the rate of degradation varied between substrates, with faster rates of degradation occurring on artificial substrates. Nui et al., (2005), modeled the quantitative structure-property relationships and concluded that the characteristics of the solution containing the PBDEs affect the photo-debromination rates.

Ahn et al., (2006), irradiated Deca-BDE bound to clays (kaolinite [$Al_2Si_2O_5(OH)_4$], montmorillonite [$Na_{0.2}Ca_{0.1}Al_2Si_4O_{10}(OH)_2(H_2O)_{10}$]) with lamps (350±50 nm, four 24-W bulbs, 14 days) or sunlight and found that numerous lesser brominated congeners (Tri- to Nona-BDEs) were formed. Ahn et al., concluded that sunlight irradiation of Deca-BDE attached to clay particulates in the atmosphere may be a significant debromination pathway. Starting with a mixture of PBDE congeners, Sánchez-Prado et al., (2005a), found similar photodebromination results, as Ahn et al., on artificial substrates and in aqueous solutions. Sánchez-Prado et al., (2005b), also found the formation of brominated dibenzofurans. The half-life ($t_{1/2}$) of Deca0BDE was longer in sunlight (261-408 days) as compared to lamp irradiation (36-44 days). Debromination also occurred in sediments ($t_{1/2}$=150 days lamp, 990 days).

Eriksson et al., (2004b), suggested that one factor in the rate of degradation is the ability of the solvent to be a hydrogen ion donor. Bezares-Cruz et al., (2004), placed hexane spiked Deca-BDE solutions in direct sunlight during the summer and found 43 PBDE breakdown products were formed. Twenty Nona- to Tetra-congeners were identified (208, 207, 206 [Nona]; 197, 196 [Octa]; 183 [Hepta]; 154, 153, 138 [Hexa]; 118, 100, 99, 85 [Penta]; 77, 71, 66, 49, 47 [Tetra]; 37, 33, 28 [Tri]) (Bezares-Cruz et al., 2004). The progression of degradation was observed to start with declining concentration of Deca and increasing concentrations of Nona-congeners followed by increasing concentrations of Octa-, Hepta-, and Hexa-congeners (Bezares-Cruz et al., 2004). Eriksson et al., (2004b), and Sánchez-Prado et al., (2005a, 2005b), observed that the progression of degradation was slower for less brominated congeners. The observed degradation rate difference between the fastest reacting PBDE (209) and the slowest (77) was 700 times. This suggests that the lower brominated congeners like Hexa-, Penta-, and Tetra-homolog will exist longer and allow for more opportunity to bioaccumulate into biota.

Degradation under anaerobic conditions (unrelated to photolytic degradation) has also been demonstrated and involved bacterial activity. Gerecke et al., (2005), demonstrated that anaerobic degradation of Deca-BDE occurs and can degrade up to 30% of Deca-BDE to lower PBDE congeners over a 238-day period. No degradation occurred under sterile conditions. The degradation products differed from those found in the Penta- and Octa-technical mixtures.

He et al., (2006), studied the ability of anaerobic bacterial cultures (*Sulfurospirillum multivorans* and *Dehalicoccoides* species) to debrominate Deca-BDE and the Octa-BDE mixture. *Sulfurospirillum multivorans* only debrominated Deca-BDE and resulted in Hepta- and Octa-BDEs being generated. After two months, Deca-BDE was no longer detectable in the *Sulfurospirillum multivorans* cultures. *Sulfurospirillum multivorans* did not degrade the Octa-BDE mixture. *Dehalicoccoides* species did not degrade Deca-BDE, but did degrade the Octa-BDE mixture to Hepta- through Di-BDEs. This included the generation of BDE-154, BDE-99, BDE-49, and BDE-47. Concentrations of the Hepta- through Di-BDEs continued to increase throughout the one year study, with Tetra-BDEs appearing after six months. The combination of these bacteria into a single culture resulted in increased rates of debromination and resulted in the additional formation of lower brominated congeners (He et al., 2006).

LEVELS IN THE ENVIRONMENT

Levels in Biota and Food Products

Biota

A recent study by the U.S. EPA for PBDEs in fish from the Great Lakes found BDE-47, 99, 100 to be the most prevalent congeners. Great Lake states collected whole lake trout from Lakes Superior, Huron, Michigan, and Ontario; whole walleye from Lake Erie; and Coho and Chinook salmon from Lakes Erie, Michigan, and Huron for the U.S. EPA study. Table 4 provides the initial results of that study.

Table 4: Average Concentrations (ng/g) of PBDEs in Fish Collected from the Great Lakes in 2000 by the U.S. EPA (Hellman, 2003)

Species	Lake	BDE 47	BDE 66	BDE 99	BDE 100	BDE 153	BDE 154
Lake Trout	Superior	79.3	3.4	52.6	18.6	8.8	15.6
Lake Trout	Huron	49	1	11	10	1	6
Lake Trout	Michigan	228	4	48	45	11	19
Walleye	Erie	32.3	0	5.9	7.8	2.6	2.4
Lake Trout	Ontario	144	2	34	24	10	13
Coho Salmon	Erie	9.5	0.1	1.0	1.2	0.5	0.8
Coho Salmon	Michigan	35.4	0	9.2	7.4	1.0	1.1
Chinook Salmon	Huron	54	2	24	13	5	6

PBDEs have been detected in Great Lakes region biota (Table 5), in biota from around the globe (Table 6), and in the global food supply (Table 7). In the Great Lakes regions, the concentrations of total PBDEs reported on a lipid weight basis, range from 26 to 16,500 µg/kg. The number and selection of congeners that constituted a "total PBDE concentration" varied between authors, making concentration comparison between studies impossible, unless done on a congener-by-congener basis.

Table 5: Total PBDE Concentrations in a Variety of Laurentian Great Lakes Biota

Sample	Location	PBDE[a]	Congeners[b]	Reference
Sunfish	Lake Hadley, Indiana	2,400	**47, 99, 100, 153, 154**, 190, 209	Dodder et al., 2002
Salmon (Chinook/Coho)	Lake Michigan	773 - 8,120	28, **47, 66,** 85**, 99, 100**, 138, **153, 154**	Manchester-Neesvig, 2001
Steelhead Trout	Lake Michigan	3000	**47, 99, 100**[c]	Asplund et al., 1999[d]
Lake Trout	Lake Ontario	540	Di- to Hepta-[e]	Alaee et al., 1999[d]
Lake Trout	Lake Ontario	945[f]	**47, 66, 99, 100, 153**[g]	Luross et al., 2000
Lake Trout	Lake Superior	140	Di- to Hepta-[e]	Alaee et al., 1999[d]
Lake Trout	Lake Superior	392[h]	**47, 66, 99, 100, 153**[g]	Luross et al., 2000
Lake Trout	Lake Huron	240	Di- to Hepta-[e]	Alaee et al., 1999[d]
Lake Trout	Lake Huron	251[h]	**47, 66, 99, 100, 153**[g]	Luross et al., 2000
Lake Trout	Lake Erie	117[h]	**47, 66, 99, 100, 153**[g]	Luross et al., 2000
Carp	De Plains River, Illinois	73.5-685	**47, 99, 100, 153, 154, 181, 183, 190**[i]	Rice et al., 2002
Carp	Lake St. Clair, Michigan	4,350[l]	**28**, **47**, 66, 85, 99, **100,** 138, 153, **154**, 183, 209	MDCH, 2006
Largemouth Bass	Detroit River	86-275	**47, 99, 100, 153, 154, 181, 183**, 190[i]	Rice et al., 2002
Northern Pike	Lake St. Clair, Michigan	18,843[l]	**28**, **47**, **66**, 85, **99**, **100,** 138, **153**, **154**, **183**, 209	MDCH, 2006
Shrimp	St. Lawrence River	26.7	28, **47**, 49, 66, **99**, **100**, 153, 154, 155, 183[j]	Law et al., 2003
American eel	St. Lawrence River	421	28, **47**, 49, 66, **99**, **100**, 153, 154, 155, 183[j]	Law et al., 2003
Greenland Halibut	St. Lawrence River	178	28, **47**, 49, 66, **99**, **100**, 153, 154, 155, 183[j]	Law et al., 2003
Herring Gull eggs	Across the Great Lakes Region	1,830 – 16,500	**28, 47, 99, 100, 153, 154, 183**[k]	Norstrom et al., 2002

[a] Total PBDE concentrations reported as "μg PBDEs/Kg lipid", unless otherwise noted.
[b] Individual congeners that were determined (i.e., analyzed for) by the authors with the numbers in bold indicating those detected and used to calculate the total PBDE concentration unless otherwise noted.
[c] Additional congeners analyzed and added to the total PBDE concentration according to Table 14 in de Wit (2002); Deca-BDE was measured.
[d] Referenced as reported in de Wit (2002).
[e] Specific congeners not listed in de Wit (2002); sum of Di- to Hepta-BDEs.
[f] Lake trout were collected in 1998.
[g] Five congeners were detected out of 24 measured; the 19 undetected congeners were not listed by the authors.
[h] Lake trout were collected in 1993.
[l] Samples were initially screened for 40 PBDE congeners between Mono- and Hepta-BDE; congeners over 5% of total were quantified.
[j] BDE-47, -99, -100 averaged 84% of the total PBDE concentration across 15 different species reported in Law et al., 2003; BDE-28, 49, 66, 153, 154, 155, 183 were determined but the results of each congener were not stated by the authors and some of these may not have been detected.
[k] 25 Di- to Hepta-BDE congeners were identified. No Mono-, Octa-, Nona-, or Deca- BDEs were found at the detection limit (0.01-0.05 ng/g wwt.). The seven congeners listed make up 97.5 $\pm$ 0.5% of the total PBDE concentration. BDE-15, 17, 49, 66, 85, 119, 140, and 155 were also quantified and 10 additional congeners were not identified.
[l] Value present as pg/g fish tissue

Table 6: Total PBDE Concentrations in a Variety of Global Aquatic and Terrestrial Biota

Sample	Location	PBDE[a]	Congeners[b]	Reference
Cow's Milk	Germany	2.5-4.5	**47, 99, 100**[c]	Kruger, 1988[d]
Chickens	Fargo, ND Store Purchased	0.5	**47, 99, 100, 153, 154, 183**	Huwe et al., 2000
Chicken Fat	AK & TX, USA	1.9-46	17, 25, 33, **47**, 66, **85, 99, 100**, 138, 140, **153, 154, 183, 209**	Huwe et al., 2002
Moose	Sweden	1.7	**47, 99, 100**[c]	Sellstrom et al., 1993; Sellstrom, 1996[d]
Reindeer	Sweden	0.47	**47, 99, 100**	Sellstrom et al., 1993; Sellstrom 1996[d]
Starlings (juvenile)	Sweden	5.7-13	**47, 99, 100**	Sellstrom et al., 1993; Sellstrom, 1996[d]
Cormorant	England, UK	300-6,400	**47, 99, 100**[c]	Allchin et al., 2000[d]
Osprey	Sweden	2,140	**47, 99, 100**	Sellstrom et al., 1993; Sellstrom, 1996[d]
Herring	Baltic Sea	3.2-61	**47, 99, 100**	Sellstrom et al., 1993; Sellstrom, 1996[d] Haglund et al., 1997[d]
Salmon	Baltic Sea	86-290	**47, 99, 100**[c]	Burreau et al., 1999; Asplund et al., 1999; Haglund et al., 1997[d]
Salmon	Japan	46	**47, 99, 100**[c]	Ohta et al., 2000[d]
Frog Livers	Scandinavian Peninsula	0.026 - .123 wwt[e]	**47**	Ter Schure et al., 2002[f]
Porpoises Blubber	England & Wales	n.d. – 6,200	**28, 47, 66, 71, 75, 77, 85, 99, 100, 119, 138, 153, 154, 190**	Law et al., 2002
Cormorant Livers	England & Wales	0.03 – 4.5	**28, 47, 66, 71, 75, 77, 85, 99, 100, 119, 138, 153, 154, 190**	Law et al., 2002
Mussels	Netherlands	0.7-17 (47) dw[g] 0.3-11 (99) dw[g] 0.1-1.5 (153) dw[g]	**47**, 85**, 99,** 138**, 153,** 209	de Boer et al., 2003[f]
Mussels	Singapore	2.1 –38 dw[g]	17, 28, 32, 35, 37, **47**, **49**, **66**, 71, 75, 85, **99**, **100**, 119, 138, **153, 154**, 166, 181, 190[h]	Bayen et al., 2003
Whales	Netherlands	35-263 wwt[e]	**47, 99, 100, 153**	Law et al., 2003
Seals	England, Wales, Australia, Azerbaijan	n.d. – 2020 wwt[e]	**47, 99, 100, 153**	Law et al., 2003
Buzzards	Flanders, Belgium	Mean $_{Total}$ = 180	**28, 47, 99, 100, 153, 154, 183**	Voorspoels et al., 2004
Sparrowhawks	Flanders, Belgium	Mean $_{Total}$ = 1,600	**28, 47, 99, 100, 153, 154, 183**	Voorspoels et al., 2004
Owls	Flanders, Belgium	Mean $_{Total}$ = 190	**28, 47, 99, 100, 153, 154, 183**	Voorspoels et al., 2004
Owl Eggs	Charleroi, Belgium	29 - 572	**28, 47, 99, 100, 153, 154, 183**	Jaspers et al., 2005

Table 6: Total PBDE Concentrations in a Variety of Global Aquatic and Terrestrial Biota
(Continued)

Sample	Location	PBDE[a]	Congeners[b]	Reference
Seabird Eggs	San Francisco, CA	1,270 – 63,300	**28, 33, 47, 66, 99, 100, 153, 154**	She et al., 2004
Peregrine Falcon Eggs	Southern Sweden	Mean $_{Total}$ = 3,800 Mean $_{BDE-209}$ = 130	**47, 99, 100, 153, 154, 183, 209**	Lindberg et al., 2004
Peregrine Falcon Eggs	Northern Sweden	Mean $_{Total}$ = 4,500 Mean $_{BDE-209}$ = 110	**47, 99, 100, 153, 154, 183, 209**	Lindberg et al., 2004
Black Guillemot	East Greenland	43 – 150	17, **28, 47**, **49, 66**, 85, **99**, **100**, **153, 154,** 183	Vorkamp et al., 2004
Ringed Seal	East Greenland	21 – 74	**17, 28, 47**, **49, 66**, 85, **99**, **100**, **153, 154,** 183	Vorkamp et al., 2004
Sculpin	East Greenland	4.2 – 17	17, **28, 47**, **49, 66**, 85, **99**, **100**, **153, 154,** 183	Vorkamp et al., 2004
Arctic Char	East Greenland	3.3 - 270	17, **28, 47**, **49, 66**, 85, **99**, **100**, **153, 154,** 183	Vorkamp et al., 2004
Trout	Greenland & N. European Mountains	4.8 – 180	1, 2, 3, 7, 8, 10, 11, 12, 13, 15, 17, 25, 28, 30, 32, 33, 35, 37, **47**, 49, 66, 71, 75, 77, 85, **99**, **100**, 105, 116, 118, 119, 126, 138, **153, 154**, 155, 166, 181, 183, 190	Vives et al., 2004
Skipjack Tuna	Global	n.d. - 53	3, **15, 28, 47, 99, 100, 138, 153, 154**, **183**, 209	Ueno et al., 2004
Barbel (fish)	Cinca River, Spain	1.3 – 298 wwt[e]	**15, 17, 25, 28, 33, 35, 37, 47, 66, 99, 100, 118, 119, 153, 154**, **183**, 209	Eljarrat et al., 2004.
Barbel Liver	Cinca River, Spain	0.2 – 280 wwt[e]	**15, 17, 25, 28, 33, 35, 37, 47, 66, 99, 100, 118, 119, 153, 154**, **183**, 209	Eljarrat et al., 2004.
Roach	Baltic Sea	64 (sum of medians) (BDE-209= 48)	17, 25, **28, 35, 47, 49**, 66, 85, **99**, **100**, 138, **153, 154**, 155, **183**, 203**, 209**	Burreau et al., 2004
Perch	Baltic Sea	20 (sum of medians) (BDE-209= 1.3)	17, 25, **28, 35, 47, 49**, **66**, 85, **99**, **100**, 138, **153, 154**, 155, **183**, **203, 209**	Burreau et al., 2004
Pike	Baltic Sea	127 (sum of medians) (BDE-209= 1.7)	17, 25, **28, 35, 47, 49**, **66**, 85, **99**, **100**, 138, **153, 154**, 155, **183**, **203, 209**	Burreau et al., 2004
Bivalves	San Francisco, CA	0 – 13,950	17, 28, 33, **47**, 66, 82, 85, **99**, **100**, 138, 153, 154, 166, 183, 190, 203, 204, 205, 206, 207, 208, 209[h]	Oros et al., 2005
Grizzly Bears	British Columbia	1.1 -535	**47, 99, 100, 153, 206, 207, 208, 209** (other not listed in paper)	Christensen et al., 2005

Table 6: Total PBDE Concentrations in a Variety of Global Aquatic and Terrestrial Biota
(Continued)

Sample	Location	PBDE[a]	Congeners[b]	Reference
Barn Owls	Belgium	Total median [liver] =1,600; Median [liver]$_{BDE-209}$ = 59; Total median [muscle] =1,400 Median [muscle] $_{BDE-209}$ = 68	**28, 47, 99, 100, 154, 153, 183, 209**	Jaspers et al., 2006
Long-eared Owl	Belgium	Total median [liver] =360 Median [liver]$_{BDE-209}$ = 66 Total median [muscle] =550 Median [muscle] $_{BDE-209}$ = nd	28**, 47, 99, 100, 154, 153, 183, 209**	Jaspers et al., 2006
Sparrowhawk	Belgium	Total median [liver] =3,100 Median [liver]$_{BDE-209}$ = 52 Total median [muscle] =2,200 Median [muscle] $_{BDE-209}$ = nd	**28, 47, 99, 100, 154, 153, 183, 209**	Jaspers et al., 2006
Kestrel	Belgium	Total median [liver] = 85 Median [liver]$_{BDE-209}$ = 58 Total median [muscle] = 62 Median [muscle] $_{BDE-209}$ = nd	28**, 47, 99, 100, 154, 153, 183, 209**	Jaspers et al., 2006
Moss	Norway	Total = 0.029-0.31 wwt[e] BDE-209 = 0.025-0.12 wwt	**28, 47, 99, 100, 154, 153, 183, 209**	de Wit et al., 2006[i]
Grouse	Norway	Total = 1.3 BDE-209 = 0.5	**28, 47, 99, 100, 154, 153, 183, 209**	de Wit et al., 2006[i]
Lynx	Norway	Total = 11.5 - 50 BDE-209 = 1 - 4	**28, 47, 99, 100, 154, 153, 183, 209**	de Wit et al., 2006[i]
Moose	Norway	Total 1.7 BDE-209 = 0.8	**28, 47, 99, 100, 154, 153, 183, 209**	de Wit et al., 2006[i]

[a] Total PBDE concentrations reported as μg PBDEs/Kg lipid, unless otherwise noted.
[b] Individual congeners that were determined (i.e., analyzed for) by the authors; the numbers in bold indicate those detected and used to calculate the total PBDE concentration unless otherwise noted.
[c] Additional congeners analyzed and added to the total PBDE concentration; according to Table 14 reported in de Wit, 2002, BDE-209 was detected.
[d] Referenced as reported in de Wit, 2002.
[e] wwt: wet weight.
[f] Referenced as reported in Law et al., 2003.
[g] dw: dry weight.
[h] According to the author, congeners in bold summed for total PBDE concentration, other congeners accounted for <1% or were not detected.
[i] Review article, see article for original citations

Table 7: Total PBDEs in Food Products from Various Locations

Food Product	Location	Congeners	Total PBDE pg/g wwt	Citation
Milk Products-liquid	Finland	47, 99, 100, 153, 154	0.82-2.0	Kiviranta et al., 2004
Milk Products-solid	Finland	47, 99, 100, 153, 154	34-40	Kiviranta et al., 2004
Fish	Finland	47, 99, 100, 153, 154	13-15	Kiviranta et al., 2004
Meat & Eggs	Finland	47, 99, 100, 153, 154	180-220	Kiviranta et al., 2004
Fats	Finland	47, 99, 100, 153, 154	15	Kiviranta et al., 2004
Cereal Products	Finland	47, 99, 100, 153, 154	1.3- 1.4	Kiviranta et al., 2004
Potato Products	Finland	47, 99, 100, 153, 154	17	Kiviranta et al., 2004
Vegetables	Finland	47, 99, 100, 153, 154	3.8- 4.2	Kiviranta et al., 2004
Fruits and Berries	Finland	47, 99, 100, 153, 154	5.4-5.5	Kiviranta et al., 2004
Fish	TX, USA	17, 28, 47, 66, 77, 85, 99, 100, 138, 153, 154, 183, 209	8.5 – 3,078	Schecter et al., 2004
Meat	TX, USA	17, 28, 47, 66, 77, 85, 99, 100, 138, 153, 154, 183, 209	0.9 – 679	Schecter et al., 2004
Dairy Products	TX, USA	17, 28, 47, 66, 77, 85, 99, 100, 138, 153, 154, 183, 209	0.2 – 1,373	Schecter et al., 2004
Atlantic Salmon	Norway	28, 47, 99, 100, 153, 154	1,140 – 4,490	Bethune et al., 2004
Mackerel	Norway	28, 47, 99, 100, 153, 154	1,260 – 1,780	Bethune et al., 2004
Herring	Norway	28, 47, 99, 100, 153, 154	1,020 – 3,530	Bethune et al., 2004
Atlantic Halibut	Norway	28, 47, 99, 100, 153, 154	320 – 17,590	Bethune et al., 2004
Cod	Norway	28, 47, 99, 100, 153, 154	20 – 40	Bethune et al., 2004
Cod Liver	Norway	28, 47, 99, 100, 153, 154	5,170 – 9,500	Bethune et al., 2004
Blue Mussels	Norway	28, 47, 99, 100, 153, 154	60 – 250	Bethune et al., 2004
Crab	Norway	28, 47, 99, 100, 153, 154	30 – 70	Bethune et al., 2004
Crab Shell Meat	Norway	28, 47, 99, 100, 153, 154	580 – 6,960	Bethune et al., 2004
Wild Alaskan King Salmon	MD, DC, USA	28, 47, 49, 66, 71, 77, 99, 100, 119, 153, 154	40 - 1,200	Hayward et al., 2004
Farmed Atlantic Salmon	MD, DC, USA	28, 47, 49, 66, 71, 77, 99, 100, 119, 153, 154	210 – 1,500	Hayward et al., 2004
Rockfish	MD, DC, USA	28, 47, 49, 66, 71, 77, 99, 100, 119, 153, 154	1,700 - 14,000	Hayward et al., 2004
Bluefish	MD, DC, USA	28, 47, 49, 66, 71, 77, 99, 100, 119, 153, 154	610 – 36,000	Hayward et al., 2004
Wild Fish Products	CA, USA	(not listed, analyzed for 31 congeners including 209)	88 – 4,955 (0 to 94% due to Deca-BDE; μ =47%)	Luksemburg et al., 2004
Farmed Fish Products	CA, USA	(not listed, analyzed for 31 congeners including 209)	311 – 3,063 (0 to 49% due to Deca-BDE; μ =26%)	Luksemburg et al., 2004
Meat Products	CA, USA	(not listed, analyzed for 31 congeners including 209)	106 – 379 (0 to 75% due to Deca-BDE; μ =39%)	Luksemburg et al., 2004

Table 7: Total PBDEs in Food Products from Various Locations
(Continued)

Food Product	Location	Congeners	Total PBDE pg/g wwt	Citation
Fowl Products	CA, USA	(not listed, analyzed for 31 congeners including 209)	85 – 2,516 (0 to 86% due to Deca-BDE; 0=39%)	Luksemburg et al., 2004
Various Farmed and Wild Fish Species	Global	1, 2, 3, 7, 8,10,11,12,13,15, 17, 25, 28, 30, 32, 33, 35, 37, 47, 49, 66, 71,75, 77, 85, 99, 100, 105, 116, 119, 126, 138, 140, 153, 154, 155, 166, 181, 183, 190, 206, 207, 208	0 – 4,800 (estimated based on bar graph, a table not in paper)	Hites et al., 2004b,c
Various Fish Species	Germany	17, 28, 47, 66, 77, 99, 100, 153, 154, 183, 209	0.01-2.88 (BDE-209: nd – 0.04)	Paepke & Herrmann, 2004
Various Fish and Shell Fish Species	Canada	15, 17, 28, 47, 66, 71, 75, 77, 85, 99, 100, 119, 126, 138, 153, 154, 183, 190	1.3 – 5,500	Tittlemier et al., 2004
Hamburger	USA	28, 33, 47, 85, 99, 100, 153, 154, 183	nd – 2,470[a]	Huwe and Larsen 2005
Bacon	USA	28, 33, 47, 85, 99, 100, 153, 154, 183	100 – 4,620[a]	Huwe and Larsen 2005
Chicken Fat	USA	28, 33, 47, 85, 99, 100, 153, 154, 183	190 – 16,620[a]	Huwe and Larsen 2005
Pork Fat	USA	28, 33, 47, 85, 99, 100, 153, 154, 183	190 – 16,330[a]	Huwe and Larsen 2005
Beef Fat	USA	28, 33, 47, 85, 99, 100, 153, 154, 183	nd – 840[a]	Huwe and Larsen 2005
Salmon Muscle	Chile	1, 2, 3, 7, 10, 13, 15, 17, 25, 28, 35, 47, 49, 66, 71, 75, 77, 85, 99, 100, 116, 119, 126, 138, 140, 153, 154, 155, 166, 181, 183, 197, 203, 207, 209	0.9 – 2.0	Montory and Barra, 2005

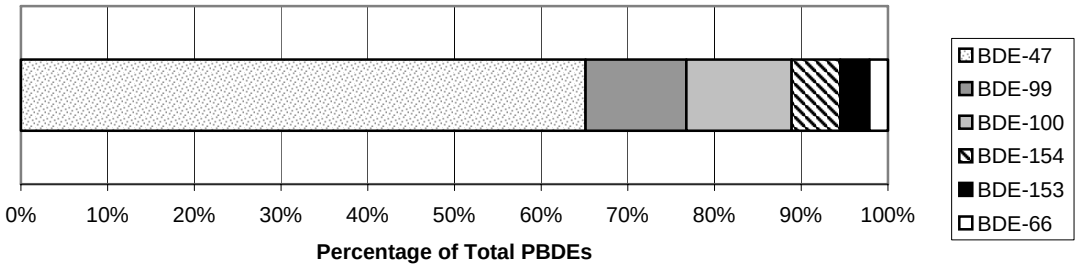
[a] concentrations are in pg/g lipid.

In general, all biota tend to have BDE-47. Aquatic biota bioaccumulate Tetra- to Hexa-homolog groups, e.g., BDE-47, 99, and 100, which make up a large percentage of the total PBDE concentrations (Lindberg et al., 2004; Dodder et al., 2002; Luross et al., 2000; Rice et al., 2002; Manchester-Neesvig et al., 2001; and Huwe et al., 2002). For example, the sum of congeners BDE-47, BDE-99, and BDE-100 were found to constitute greater than 85% of the total PBDE concentrations in Lake Michigan salmon (Figure 3) (Manchester-Neesvig et al., 2001). However, animals feeding from terrestrial food webs may be more likely to accumulate higher brominated PBDEs such as Deca-BDE (Law et al., 2003, Lindberg et al., 2004, de Wit et al., 2006). The highest levels of PBDEs in terrestrial biota are found in the top predators (de Wit et al., 2006). Grizzly bears feeding primarily from terrestrial sources had a PBDE congener profile dominated by Deca-BDE, 208, 207, and 206 (Christensen et al., 2005). Terrestrial birds of prey were shown to consistently have Deca-BDE, whereas aquatic bird species did not have

Deca-BDE (Jasper et al., 2006). Herzke et al., (2005), found low levels (range: 0.5-4 ng/g wwt) of Deca-BDE in the eggs of five Norwegian birds of prey species.

Figure 3: The Fraction of Each PBDE Congener Found in Lake Michigan Salmon (N=21) Expressed as a Percentage of the Total PBDE Concentration

(Data acquired from Manchester-Neesvig et al., 2001.)



These generalizations must be used cautiously, because many factors can influence the meaning of "total PBDE concentration." Factors such as variations in analytical methods, availability of analytical standards, or difference in species and exposure pathways may greatly influence the meaning of "total PBDE concentration." Analyses conducted more recently will be able to quantify more congeners, due to better analytical methods and materials. As of 2005, analytical standards are commercially available (Cambridge Isotope Labs) for 40 to 45 congeners out of the possible 209 congeners, but this was not true several years ago.

One potentially substantial bias may be how authors select which congeners they attempt to determine. Authors have derived different methods of selecting the congeners to determine in their samples. For example, Rice et al., (2002), screened samples for 40 congeners using Cambridge Isotope standard #EO-4980, and then quantified the most common (>5% of sample) individual congeners resulting in 7-8 congeners making up their estimate of total PBDEs. Huwe et al., (2002), screened samples using the 40 congener standard, as well as using an additional standard specifically for Deca-BDE. Huwe et al., (2002), then looked for peaks in all homolog groups between Mono- and Deca-BDEs to evaluate the comprehensiveness of the selected peaks. Manchester-Neesvig et al., (2001), selected nine congeners that the authors expected to be commonly found in the commercial mixtures and that have been observed to bioaccumulate in biota. Bayen et al., (2003), also based their selection of congeners on those commonly found in commercial mixtures. Selection bias may result in the congeners from Tetra-, Penta-, and Hexa-homolog groups, i.e., BDE-47, 99, and 100, being the most commonly reported values. Congeners from the Hepta-, Octa-, Nona-, or Deca-homolog groups may not have been analyzed for as frequently or with sufficiently sensitive detection limits. For example, Huwe et al., (2002), found congener BDE-209 made up a significant percentage of the total PBDE concentration along with BDE-47, 99, 100, 153, and 154 in chicken fat samples. Lindberg et al., (2004), recently reported the detection of BDE-183 (7% of total PBDE) and Deca-BDE (3% of total PBDE) at significant concentrations in the eggs of falcons. Rice et al., (2002), found Hepta-congeners BDE-181 and 183 in fish tissue samples. Norstrom et al., (2002), found significant quantities of BDE-183 in herring gull eggs. On the other hand,

Dodder et al., (2002), was unable to detect BDE-190 (detection limit = 2 ng/g lipid) or Deca-BDE (detection limit < 0.5 ng/g lipid). This was also true for Norstrom et al., (2002), who were unable to detect any Octa-, Nona-, or Deca-congeners (detection limits were between 0.01 and 0.05 ng/g wet weight).

Therefore, the conservative approach when evaluating concentrations in biota presented in this paper would be to avoid making distinctions between concentrations from different studies that have less than a 100-fold difference. Furthermore, the total PBDE concentrations presented in the preceding tables (refer to Tables 4 and 5) should not be used in combination to make either temporal or spatial evaluations. One can assume that these biota values demonstrate that congeners of PBDE commercial formulations are found to bioaccumulate in a wide range of biota sampled in numerous locations around the world. It appears that organisms at the top of the food chain tend to reach higher concentrations than those lower in the food chain.

Food Products

Several papers were published in 2004 reporting total PBDE concentrations in various food products from around the world (refer to Table 7). Fish products tended to have the highest concentrations followed by meat and dairy products. Luksemburg et al., (2004), found that 26-47% of the total PBDE concentration was due to Deca-BDE. Schecter et al., (2004), had a similar result from a cheese sample. These data demonstrate that PBDEs are in the food supply both in the U.S. and around the world; concentrations vary between foods and possibly between locations; and Deca-BDE is commonly found in food.

Spatial Trends of Levels in Biota

Limited data exist on global spatial trends, especially in North America (de Wit et al., 2002). Comparing PBDE concentrations in Great Lakes fish tissue, Lake Michigan lake trout (mean=1,400 ng/g lipid) had the highest mean concentrations, followed by Lake Superior lake trout (mean=999 ng/g lipid), Lake Erie walleye (mean=600 ng/g lipid), Lake Ontario lake trout (mean=550 ng/g lipid), and Lake Huron lake trout (mean=370 ng/g lipid) (Zhu and Hite, 2004).

Most monitoring data have been collected in Europe, which has allowed for some evaluation of spatial tends. Current evidence suggests that the coastline of southern Europe is the most contaminated with PBDEs followed by the Baltic Sea with the lowest levels in the Arctic (de Wit, 2002). This pattern is similar to the one observed for other persistent and bioaccumulative chemicals, such as dichlorodiphenyltrichloroethane and PCBs.

Ueno et al., (2004), found that skipjack tuna populations nearer to emerging industrial countries showed higher PBDE concentrations. Proximity to industrialized areas is one factor in determining concentrations in biota.

Researchers in Sweden found that freshwater fish in southern Sweden were more contaminated with PBDEs than fish in northern Sweden (Sellstrom, 1996, as cited in de Wit et al., 2002). Concentrations of PBDEs in cod liver were found to be decreasing from more southern portions of the North Sea compared to more northern portions (de Boer, 1989, as cited in de Wit et al., 2002). Bytingsvik et al., (2004), found cod from the southern parts of the North Sea to be considerably lower in PBDE concentrations than cod from the Atlantic Ocean, and this difference is likely due to proximity to higher population density areas. It would appear that colder climates may have slightly lower PBDE concentrations in aquatic biota. Wolkers et al., (2004), also observed PBDEs in Arctic food chains demonstrating the global nature of these

chemicals. Vorkamp et al., (2004a), observed similar spatial trends of PBDEs as other persistent organic pollutants in Greenland. Ueno et al., (2004), also observed in colder climates a higher ratio of BDE-28 and BDE-47 and lower proportions of BDE-99, BDE-153, and BDE-154.

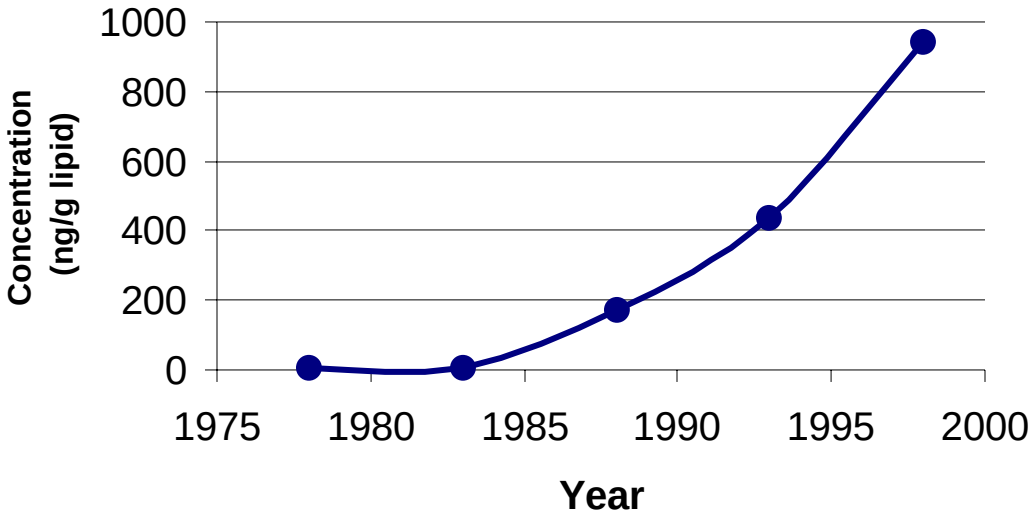
Temporal Trends of Levels in Biota

Monitoring chemical contamination in the same species over many years is a very effective method for determining and tracking trends. These methods work especially well for persistent and bioaccumulative chemicals such as PBDEs. Biota monitoring for temporal trends is most convincing when different species that have differing life histories exhibit similar chemical contaminant trends. Having multiple species showing similar temporal trends indicates that those trends are documenting actual changes in the environment and are not due to changes in food web structure or analytical anomalies.

For PBDEs, multiple species with different life histories and from different locations around the globe have been analyzed and show similar increasing trends over the past two decades. The Swedish National Environmental Monitoring Program analyzed pike from Lake Bolmen and found a six-fold increase in BDE-47, 99, and 100 between 1980 and 1987 (de Wit, 2002). A similar increasing trend was observed in Lake Ontario lake trout between 1978 (3 ng/g lipid) and 1998 (945 ng/g lipid) showing a 300-fold increase in total PBDEs (Figure 4) (Luross et al., 2000). Also in the Great Lakes, Zhu and Hites (2004), analyzed lake trout samples from 1980 to 2000 from Lakes Superior, Michigan, Huron, and Ontario and walleye from Lake Erie for 14 PBDE congeners (17, 28, 47, 49, 66, 71, 85, 99, 100, 138, 153, 154, 183, and 209). The sum of these PBDE congeners increased exponentially in all the Great Lakes from 1980 to 2000, with doubling times ranging between 3-4 years. The sum of the congeners BDE-47, 99, and 100 increased in proportion to BDE-153 and 154. Canadian researchers found PBDEs in landlocked Canadian arctic char to be increasing annually between 1997 and 2002, with mean concentrations in 2001 and 2002, being significantly higher than in 1997 (de Wit et al., 2006).

Sellstrom et al., (2003), monitored concentrations of BDE-47, BDE-99, and BDE-100 in guillemot eggs from the Baltic Sea. Concentrations were increasing from 1969 to the mid-1980s. These congeners reached peak concentrations during the middle to late 1980s. Steep declines in these three congeners were observed during the 1990s. Sellstrom et al., (2003), note that their findings disagree with other studies in Sweden over the same timeframe and that these declines could be due to a different exposure route. These findings may also reflect the voluntary discontinuation of PBDEs by the Association of German Chemical Industry in 1989. Herring gull eggs from the Great Lakes region analyzed by the Canadian government showed a 60-fold increase during the past two decades with no significant signs of downward trends (Moisey et al., 2001, as cited in de Wit, 2002). Elliott et al., (2005) analyzed eggs from great blue herons (1987-2002), and double-crested cormorants (1979-2002), from British Columbia, Canada for eight PBDE congeners (28, 47, 49, 99, 100, 153, 154, and 183). The most prevalent congeners (47, 100, 99, 153, and 154) in both species showed increasing trends into the mid-1990s, and then declined during the late 1990s. Concentrations in cormorant eggs continued to decline in 2002, however, the herons had increasing concentrations in 2000 (100, 153) and 2002 (47, 49, 99, 100, 153, and 154), with the highest total PBDE concentrations of the dataset being recorded in 2002. Additionally, increasing temporal trends (5-10% per year) of BDE-47, 49, 85, 99, 100, 153, 183, and 209 in peregrine falcon eggs from 1981 to 2003 were documented in South Greenland (Vorkamp et al., 2005).

Figure 4: Total PBDE Concentrations in Whole Lake Trout from Lake Ontario Between 1978 and 1998 (Luross et al., 2000)



Marine mammals also appear to be exhibiting a similar increase in PBDEs. Ikonomou et al., (2002), reported that blubber from ringed seals around Holman Island in the Northwest Territories of the Canadian Arctic increased in PBDEs from 0.572 ng/g lipids in 1981 to 4.62 ng/g lipids in 2000. Kajiwara et al., (2004), analyzed for 10 PBDE congeners (BDE-3, 15, 28, 47, 99 100, 153, 154, 183, 209) in fat/blubber from northern fur seals collected off the northern coast of Japan from 1972 to 1998. From 1972 to 1991, the concentrations were increasing with peak concentrations occurring between 1991 and 1994. The concentrations in 1998 were 50% less than the peak years. Kajiwara et al., (2004), observed an increase in higher brominated congeners with a decrease in some lower brominated congeners. Blubber from beluga whales in the Cumberland Sound of the Canadian Arctic also showed a similar increasing trend between 1982 (2.11 $\pm$ 0.38 ng/g lipid) and 1997 (14.6 $\pm$ 7.09 ng/g lipid) (Law et al., 2003). Additional beluga whale blubber samples were analyzed from the eastern Canadian Arctic for 2001, showing concentrations continuing to increase to approximately 25 ng/g lipid (de Wit et al., 2006). Furthermore, a trend in beluga whale blubber from southeast Baffin, Canada was observed between 1982 (2 ng/g lipid) and 1996 (15 ng/g lipid) (Stern and Ikonomou, 2000, as cited in Law et al., 2003). LeBeuf et al., (2004), analyzed 54 beluga whale blubber samples from 1988-1999 and identified BDE-congener (28, 47, 49, 66, 99, 100, 153, 154, 155, and 183) with BDE-47, 99, and 100 contributing 75% of the total PBDE concentration. Total PBDE concentrations increased exponentially between 1988 and 1999, with a doubling time of three years or less. The Tri-, Hexa-, and Hepta-congeners comprised a smaller percentage of the total PBDEs in 1999 compared to 1988, whereas the Tetra- and Penta-congeners comprised the same or greater percentage over the same time period. Two species of dolphins were sampled for PBDEs in blubber from the northeast coast of the U.S. The number of samples were limited, but covered the years 1993 to 2000. No increasing or decreasing trend in PBDE concentrations was observed (Tuerk et al., 2005).

In the United Kingdom, Hassanin et al., (2005), reported PBDE concentrations in herbage between the early 1900s and 2004, with concentrations increasing over that time and generally

following estimated emissions. Peak concentrations in the herbage appear to have occurred in both 1984 and 1999 with some suggestion of declining trends between 2000 and 2004. Hassanin et al., (2005), noted that concentrations of BDE-28 were increasing between 1999 and 2004.

PBDE concentrations in multiple species showing substantial increasing trends over the past two decades have raised the level of interest by both scientists and the public to gain a better understanding into the potential significance of these global increases. As several authors stated, current PBDE concentrations do not typically exceed the current PCB concentrations in the same organism, however, PCBs have generally been declining in biota over the past three decades since PCBs were banned in the U.S. during the 1970s, whereas PBDEs appear to be increasing in biota. Since further studies into the temporal trends of PBDEs in Great Lakes biota are warranted, the Office of the Great Lakes awarded the U.S. Geological Survey a grant to analyze archived samples of smelt from the 1980s and 1990s to determine temporal trends in the concentrations of PBDEs.

Levels in Humans

A growing amount of information is becoming available on PBDE levels in human tissues from people living in North America. This includes data on analyses of archived samples from the past as well as data on more current samples. These data show that levels in human tissues in North America have increased significantly over time, and are much higher compared to levels in Europe or Japan.

Blood

The earliest data for blood levels in the U.S. comes from a study that analyzed archived serum samples from blood that had been collected between 1959 and 1966 (Petreas et al., 2003). The archived samples came from 420 mothers living in the San Francisco Bay area who had been recruited for an epidemiology study investigating developmental effects and in utero exposure to organochlorine pesticides. Due to the small serum sample size, only BDE-47 could be analyzed, and the detection limit was relatively high (10 ng/g lipid). BDE-47 was not detected in any of these samples.

Sjodin et al., (2001), analyzed archived serum samples from twelve blood donors collected at a commercial blood collection facility in the state of Illinois. The blood was collected in 1988. Concentrations of BDE-47 ranged from <0.4-23.8 ng/g lipid, with a median reported value of 0.6 ng/g lipid. BDE-47 was found in 50% of the samples. Six other PBDE congeners were identified and quantified, and concentrations of six additional structurally unknown congeners (Octa- and Nona-BDEs) were estimated using the response factor for BDE-203. The concentrations of the identified congeners are listed in Table 8.

Table 8: PBDE Concentrations in Serum Samples (collected in 1988) from an Illinois Blood Collection Facility (Sjodin et al., 2001)

PBDE Congener	Median (ng/g lipid)	Range (ng/g lipid)
BDE-47	0.6	<0.4 – 23.8
BDE-99	0.3	<0.2 – 3.7
BDE-100	0.2	<0.1 – 2.4
BDE-153	0.3	0.08 – 2.0
BDE-183	0.2	0.09 – 1.3
BDE-203	<0.08	<0.08 – 0.2
BDE-209	<1.0	<1.0 – 33.6

Petreas et al., (2003), reported on serum levels of BDE-47 in 50 Laotian immigrant women, of ages 19 to 40 years old, from samples collected between 1997 and 1999. Due to the small serum sample size available for analysis, only BDE-47 was measured, and the limit of detection was relatively high (10 ng/g lipid). The BDE-47 levels ranged from non-detectable (<10 ng/g lipid) to 511 ng/g lipid, with a mean concentration of 50.6 ng/g lipid. A total of 48% of the samples had detectable levels above the reporting limit of 10 ng/g lipid.

Mazdai et al., (2003), measured levels of six congeners of PBDEs in 12 pairs of maternal serum and cord blood samples taken during the year 2001. The congeners analyzed included the following: BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, and BDE-183. The participants in this study lived in the Indianapolis area. The maternal sera levels of total PBDEs ranged from 15-580 ng/g lipids, and the fetal cord sera levels ranged from 14-460 ng/g lipid. The individual fetal sera concentrations did not differ significantly from the maternal levels, indicating measurement of maternal PBDE levels is useful for predicting fetal exposure. The congener found at the greatest concentration was BDE-47, and consisted of 53-64% of the total PBDE in serum. BDE-99 was the next most abundant congener and was present at 15-19% of the total PBDEs. The concentrations in maternal and fetal samples were found to be 20-106 times higher than levels previously reported in a similar population of Swedish mothers and infants.

Compared to the data reported by Mazdai et al., (2003), lower levels of PBDEs were found by Houlihan et al., (2005), in ten cord blood samples taken from live births at U.S. hospitals between August and September 2004. The cord blood samples were analyzed for 46 different PBDE congeners, and a total of 32 different congeners were found in the samples. Total PBDEs ranged from 1.11-14.2 ng/g (lipid weight, in whole blood) with an average concentration of 6.42 ng/g lipid. BDE-47 was found in 4 out of 10 samples at concentrations of 0.33-3.79 ng/g lipid. BDE-99 was found in four out of ten samples at concentrations of 0.087 to 0.681 ng/g lipid. BDE-153 was found in 10 out of 10 samples with concentrations of 0.24-7.47 ng/g lipid. Deca-BDE was found in 3 out of 10 samples at concentrations of 0.43-9.63 ng/g lipid.

In a time trend analysis, six PBDEs (BDE-47, BDE-85, BDE-99, BDE-100, BDE-153, and BDE-154) were measured in 40 serum pools collected in the southeastern U.S. from 1985-2002, and in Seattle, Washington from 1999-2002 (Sjodin et al., 2004). The serum pools from the southeastern U.S. were collected from an interstate blood bank and consisted of samples from 40-200 donors. The serum pools from Seattle were collected from a research laboratory and consisted of samples from 6-8 donors. The results are presented as five year collection

periods, and show that for all PBDEs, except BDE-85, the concentrations increased significantly from 1985-2002. BDE-47 was found at the highest concentrations, with reported median levels of 5.4, 28, 46, and 34 ng/g lipids for the periods of 1985-1989, 1990-1994, 1995-1999, and 2000-2002, respectively. Median levels for total PBDEs for these same time periods were 9.6, 48, 71, and 61 ng/g lipid.

Schecter et al., (2005a), provided a comparison of PBDE levels in a pooled serum sample from 100 Dallas, Texas research subjects that had been collected in 1973, with that of various blood samples taken in 2003, including a pooled serum and blood sample (n = 100) from Dallas, Texas, and whole blood samples from 29 individuals in Mississippi, and ten from New York City. A total of 13 individual congeners were analyzed for each of the samples. In the 1973 pooled serum sample, no PBDE congeners were detected. Total PBDEs are reported as 0.77 ng/g lipid, based on half the detection limit. In contrast, PBDEs were detected in all the samples from 2003. Levels of BDE-47, BDE-99, BDE-153, and total PBDEs are shown in Table 9.

Table 9: PBDE Levels in United States Human Blood (ng/g lipid)*

Congener	1973 Serum Pool	2003 Serum Pool	2003 Whole Blood Pool	2003 Whole Blood Mean (Individual Analyses) (n=39)	2003 Whole Blood Median (Individual Analyses) (n=39)
BDE-47	ND	32.5	44.2	25.0	12.8
BDE-99	ND	8.4	12.8	11.1	3.2
BDE-153	ND	12.3	11.7	5.7	3.6
BDE-209	ND	NA	1.4	2.7	2.3
Total	0.77	61.84	79.7	52.6	29.6

*Schecter et al., (2005a); ND = Not detected; NA = Not available

For the 39 individual blood samples, total PBDE levels ranged from 4.6-192.8 ng/g lipids in men, compared to 5.6-365.5 ng/g lipids in women. Mean and median values of total PBDEs in women were higher than in men, but the differences were not statistically significant. Mean levels were 35.9 ng/g lipids in men, compared to 74.1 ng/g in women. Median levels were 25.1 ng/g lipid in men and 43.3 ng/g lipid in women. No significant correlation between levels in blood and age were found.

Serum levels of PBDEs were measured in 93 urban anglers living in New York and New Jersey during 2001-2003 (Morland et al., 2005). Data for Deca-BDE could not be reported, because of high background contamination during the processing of unknown samples. BDE-47 was found at the highest concentration, with a geometric mean value of 13.29 ng/g lipid. Geometric mean concentrations of other congeners include the following: BDE-99 at 3.23 ng/g lipid, BDE-153 at 3.17 ng/g lipid, BDE-100 at 2.70 ng/g lipid, BDE-85 at 1.03 ng/g lipid, BDE-154 at 0.63 ng/g lipid, and BDE-183 at 0.53 ng/g lipid. In general, small non-statistically significant ($p < 0.05$) increases in serum PBDE levels were found in anglers who reported eating locally caught fish. The authors indicate these data suggest that consumption of locally caught fish is not a major source of exposure in this population.

The only data available for PBDE in children comes from a California newspaper that reported on serum levels from a family of four, including a toddler boy, five year old girl, 35-year old father, and 36-year old mother (Fisher, 2005 and 2006). Blood samples were taken in September 2004 and analyzed by a laboratory in Canada, and then sampled again in December 2004 and analyzed by a laboratory in Sweden. Total PBDE levels were highest in the toddler (838 parts per billion [ppb]), followed by the 5-year old girl (490 ppb), then the mother (138 ppb) and father (102 ppb). No major differences were found between the two labs and sampling dates for BDE-47, BDE-99, and BDE-100. Deca-BDE was significantly lower in the December samples compared to the September samples. A basis for the differences in Deca-BDE between the two laboratory results could not be determined. This information is shown in Table 10.

Table 10: Serum DECA-BDE Levels (ng/g lipid) in a California Family (Fisher, 2005)

Sample	Canadian Results September 2004 Sample	Swedish Results December 2004 Sample
Father	30	2.5
Mother	21	3.9
5-year old	166	10
Toddler	277	22

Serum levels of PBDES were measured in a group of Swedish rubber workers with exposure to Deca-BDE only, and compared to a reference group of slaughterhouse workers with no occupational exposure to PBDEs (Thuresson et al., 2005). Median concentration of Deca-BDE in the rubber workers was 35 ng/g lipids, compared to 2.4 ng/g lipids in the reference group. Concentrations of all Nona-BDEs and several Octa-BDEs were also elevated among the rubber workers, with median concentrations 2.5-11 fold higher than in the reference group. The authors suggest this may indicate a potential for in vivo debromination of Deca-BDE.

Breast Milk

Twenty breast milk samples from a milk bank in Vancouver, Canada that were obtained between 2001 and 2002, were analyzed for seven different PBDE congeners (Ryan et al., 2002). These included BDE-28, BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, and BDE-183. The sum total concentration of PBDEs ranged from 0.9-281.9 ng/g lipid, with a mean concentration of 42.8 ng/g lipid, and a median value of 25.4 ng/g lipid.

In a recent study by Schecter et al., (2003), milk samples from 47 nursing mothers in the Austin and Dallas, Texas area were analyzed for 10-13 PBDE congeners. The samples were collected from August to December 2002. The sum of the PBDE concentrations in individual samples ranged from 6.2-419 ng/g lipids. The median concentration was 34 ng/g lipids, and the mean concentration was 73.9 ng/g lipids. PBDE-47 was present at concentrations that ranged from 2.9-272 ng/g lipids, with a mean concentration of 40.8 ng/g and a median value of 18.4 ng/g lipid. Deca-BDE was found in 6 out of 23 samples, where this congener was measured. The levels of PBDEs found in this study were reported to be 10-100 times greater than human tissue levels in Europe. In an update of this ongoing study, Schecter et al., (2005a), reported on PBDE levels in breast milk samples taken from 59 U.S. women between the years 2001-2004.

Total PBDE levels ranged from 6.2-418.8 ng/g lipids, with a median value of 30.1 ng/g lipids, and a mean concentration of 65.9 ng/g lipids.

The Environmental Working Group (Lunder, 2003a), released a study that measured breast milk levels of PBDEs from 20 women around the U.S. The study participants were first time mothers and were recruited from November 2002 through June 2003. PBDEs were found in every breast milk sample and included up to 35 different PBDE congeners in all. The concentrations of PBDEs found in the breast milk ranged from 9.5-1078 ng/g lipid. The average concentration was 159 ng/g lipids, and the median concentration was 58 ng/g lipids. The two highest concentrations were 755 and 1078 ng/g lipid, significantly higher than any other levels previously measured in breast milk. BDE-47 accounted for about one-half of the total PBDEs in each participant's sample. This congener, along with six others, made up greater than 90% of the total PBDEs.

Breast milk samples collected from 40 healthy first time mothers living in the Pacific Northwest, whose healthy infants were between 2-8 eight weeks of age, were analyzed for 12 congeners of PBDEs (Northwest Environment Watch, 2004). The PBDE congeners included tri-PBDEs through Deca-PBDEs. The 40 mothers consisted of ten each from Montana, Oregon, Washington, and British Columbia. Samples were collected from April through November 2003. All breast milk samples contained PBDEs, with total PBDE levels ranging from 6-321 ng/g lipids. The median and mean total PBDEs were 50 and 97 ng/g lipid, respectively. Three PBDE congeners (PBDE-47, PBDE-99, and PBDE-100) accounted for at least three-quarters of the total PBDEs detected in all samples. Table 11 provides levels found for select PBDE congeners.

Table 11: Breast Milk PBDE Concentration (ng/g lipid) from Pacific Northwest Mothers (Northwest Environment Watch, 2004)

PBDE Type	Range	Median	Mean
PBDE-47	2.6 – 201	26	50
PBDE-99	0.8 – 49	5.4	10
PBDE-100	0.5 – 76	5.2	12
PBDE-153	0.8 (MDL) – 169	4.8	16
PBDE-209	0.05 (MDL) – 4.3	0.4	0.8

Levels of PBDEs in breast milk in women from Michigan are currently being investigated in a study funded by the Michigan Great Lakes Protection Fund (Karmaus and Riebow, 2003). This study is looking at breast milk levels of PBDEs in fish eaters from the communities of Benton Harbor, St. Joseph, and nearby areas. No results from this study are currently available.

Adipose Tissue

Breast adipose samples were taken from a group of 32 women, age 25-54 years old, who participated in a breast cancer study in the late 1990s and analyzed for PBDEs (Petreas et al., 2003). Samples were collected during biopsy or breast surgery between the years of 1996 and 1998. BDE-47 was the major congener found and was present in all samples. BDE-99, BDE-100, BDE-153, and BDE-154 were also reported to be measurable in all samples, however, only BDE-47 concentrations were reported in the study. The BDE-47 levels in breast adipose tissue

ranged from 5.2-196 ng/g lipids, with a mean concentration of 28.9 ng/g lipid. The median concentration was 16.5 ng/g lipids.

Breast and abdominal adipose tissues taken from 21 women undergoing mastectomies with simultaneous reconstruction were analyzed for a number of persistent lipid soluble compounds, including PBDEs to determine if concentrations measured in one tissue could predict the other (Petreas, 2004). The women were a subset of a larger breast cancer case-control study centered in the San Francisco Bay area that may be the same as discussed above (Petreas et al., 2003). Within this subset of 21 women, results for PBDEs were reported for 7-8 women. Insufficient sample size for analysis, or measurements below the limit of detection, was a basis for exclusion from the comparison analysis. The reported mean concentrations for the abdominal and breast adipose pairs were: 38, 8.8, 11, 24, and 10 ng/g lipid for BDE-47, BDE-99, BDE-100, BDE-153, and BDE-154, respectively. No statistically significant differences between breast and abdominal adipose tissue concentrations were found for all reported PBDE congeners, based on the Wilcoxon signed rank test. However, in another statistical analysis involving regression analysis to predict breast concentration from abdominal concentration, a poor fit (R2 = 0.41) was observed only for BDE-154. This indicates BDE-154 appears to partition more in the abdominal than in the breast adipose tissue.

Adipose samples from 53 patients undergoing liposuction procedures in New York City were analyzed for PBDEs (Johnson-Restrepo et al., 2005). Samples were collected from October 2003 - October 2004, and analyzed for eight known PBDE congeners (BDE-28, BDE-30, BDE-47, BDE-85, BDE-99, BDE-100, BDE-153, and BDE-154) and three unidentified di-, tri-, and penta-BDE congeners. Deca-BDE was only evaluated on a qualitative basis, but was not detected in most samples. The average age of the patients was 31 years (range: 18-51 years), and 77% were females, while 23% were males. Total PBDEs ranged from 17.4 to 9630 ng/g lipid, with a median concentration of 77.3 ng/g lipid, and a mean of 399 ng/g lipid. The adipose sample containing PBDEs at 9630 ng/g lipid is the highest concentration in any human tissue reported in the literature to date. The two highest concentrations (9630 and 4060 ng/g lipid) qualified as outliers, as they were greater than four times the standard deviation of the mean concentration. BDE-47 was found at the highest concentration and ranged from 1.3-2720 ng/g lipid, with a median of 29.3 ng/g lipids and a mean of 132 ng/g lipids. Median and mean concentrations for other congener concentrations were as follows: BDE-99 (median: 10.3 ng/g lipid; mean: 74.4 ng/g lipid), BDE-100 (median: 12.0 ng/g lipid; mean: 67.7 ng/g lipid), BDE-153 (median: <1 ng/g lipid; mean: 91/8 ng/g lipid), and BDE-154 (median: <1 ng/g lipid; mean: 8.3 ng/g lipid). PBDE concentrations in adipose tissue were not correlated with age, gender, or PCB concentrations.

Spatial and Temporal Trends

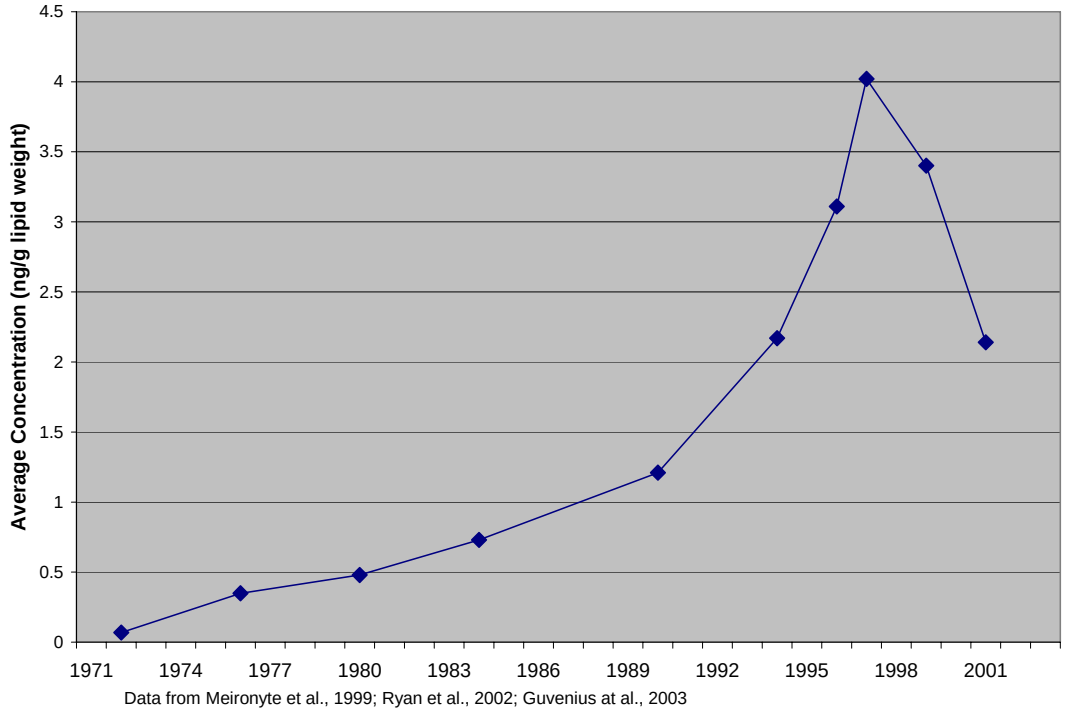
Data on concentrations of PBDEs in human blood, breast milk, and adipose levels have consistently shown levels to be significantly higher in North America compared to Europe or Japan. Table 12 provides a comparison of some of the recent data on levels of PBDEs in breast milk samples from Sweden and North America. Levels in the U.S. are the highest, with median concentrations around 25 times those found in Sweden and up to two fold higher than those found in Canada.

Table 12: Total PBDE Concentration (ng/g lipid) in Contemporary Breast Milk Samples

Country	Year	Median	Mean	Reference
Sweden	1996-1999	3.2	4.0	Ryan et al., 2002
Sweden	2000-2001	2.14	Not given	Guvenius et al., 2003
Canada	2001-2002	25.4	42.8	Ryan et al., 2002
USA (Texas)	2002	34	73.9	Schecter et al., 2003
USA	2002-2003	58	159	Lunder, 2003
USA & Canada (Pacific NW)	2003	50	97	Northwest Environmental Watch, 2004

Temporal trends show levels of PBDEs are increasing significantly over time. The most extensive data on temporal trends for breast milk levels comes from Sweden. These data are presented graphically in Figure 5. From the years 1972-1997, PBDEs in breast milk in Sweden rose steadily from 0.07-4.02 ng/g lipid (Meironyte et al., 1999). During this time period levels in breast milk in Sweden increased about 60-fold, with a doubling in concentration every five years. The most recent data from Sweden (Guvenius et al., 2003), indicate levels of PBDEs in breast milk in Sweden may now be decreasing. This decrease in breast milk appears to follow a significant reduction in usage of commercial PBDE products. From 1997-1998, the EU decreased PBDE use by two-thirds, or about 180,000 pounds (Madsen et al., 2003).

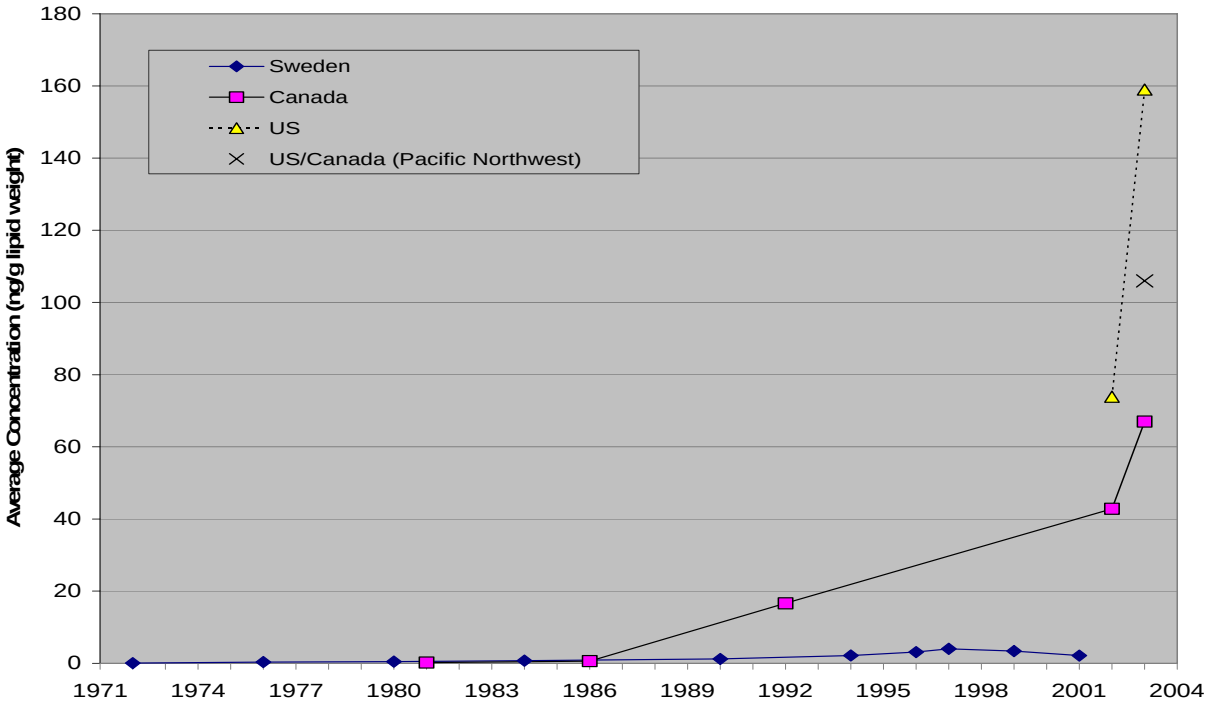
Figure 5: PBDEs in Breast Milk from Sweden, 1972-2001



Concentrations of PBDEs in North America have also shown increases over time, like in Sweden; however, levels in North America are significantly higher and appear to be continuing to rise. Levels of PBDEs in North Americans appear to be doubling every 2-5 years (Betts, 2002). Figure 6 shows the trend data for PBDE concentrations in breast milk for Sweden, Canada, and the U.S. The same Swedish data provided in Figure 5 are also included in Figure 6, however, it should be noted that the scales on the graphs differ significantly.

Figure 6: Trends of PBDEs in Human Milk for Sweden, Canada, and the United States

(Data from Meironyte et al., 1999; Ryan et al., 2002; Guvenius et al., 2003; Schecter et al., 2003; EWG, 2003; Northwest Environmental Watch, 2004)



Hites (2004a) recently reviewed and analyzed data from studies analyzing PBDE levels in people and the environment. Only data on congeners BDE-47, BDE-99, BDE-100, BDE-153, BDE-154, and Deca-BDE were included in this study. Analysis of human samples (primarily blood, breast milk, and adipose tissue) from Japan, Europe, and North America from 1970-2002, showed PBDE levels increased exponentially with a doubling time of approximately five years. In general, levels of PBDEs in people have increased by a factor of about 100-fold during this time period. This analysis also showed that levels in the Japanese population were the lowest, and the levels in the North American populations were the highest. Hites (2004a) also provided the congener distribution as average percent of total PBDEs for the human data. The data from non-occupationally exposed people showed BDE-47 made up the highest percent of the total PBDEs at about 50%, followed next by BDE-153 at about 20%, and then BDE-99, BDE-100, and BDE-154 at lower percentages. In occupationally exposed people, again BDE-47 was found at the highest percentage at about 30%; however, Deca-BDE was the second highest percent at about 25%, followed by BDE-153, BDE-99, BDE-154, and BDE-100.

Levels in Environmental Media

Outdoor Air

Limited ambient air monitoring data for PBDEs in North America are available. Table 13 provides a summary of much of this information. The earliest data available is from 1979, when Di-BDE was identified in atmospheric particulate matter near a PBDE manufacturing plant in Arkansas (Hale et al., 2003). Monitoring data from 1997-1999 in urban and remote sites in the Great Lakes region showed total PBDE levels, including particulate and gaseous concentrations, in the range of 4.4-77 pg/m^3 (Strandberg et al., 2001). The samples were collected as part of the Integrated Atmospheric Deposition Network and were taken at four different sites in the Great Lakes basin. These included Chicago, Illinois; Sleeping Bear Dunes, Michigan; Eagle Harbor, Michigan; and Sturgeon Point, New York. BDE-47 was found at the highest concentration followed by BDE-99, and then BDE-100. Mono-Tri-PBDEs were not measured in this study. The highest concentrations were found near the city of Chicago.

Table 13: Ambient Air Monitoring Data for North America

Location	Total PBDE concentration (pg/m^3)	Years	Reference
Chicago, Illinois	52 (3 year avg.)	1997 - 1999	Strandberg et al., 2001
	100 (1 year avg.)	2002 - 2003	Hoh and Hites, 2005
Eagle Harbor, Michigan	5.5 (3 year avg.)	1997 - 1999	Strandberg et al., 2001
Sleeping Bear Dunes, Michigan	15 (3 year avg.)	1997 - 1999	Strandberg et al., 2001
	16 (1 year avg.)	2002 - 2003	Hoh and Hites, 2005
Sturgeon Point, New York	7.2 (3 year avg.)	1997 - 1999	Strandberg et al., 2001
Alert, Canada	1-28	1994 - 1995	de Wit, 2002, citing Alaee et al., 1999
Ottawa, Canada	2.2 (mean) 2.6 (median)	Dec. 2002 - March 2003	Wilford et al., 2004a
Bloomington, Indiana	19 (1 year avg.)	2002 - 2003	Hoh and Hites, 2005
Rohwer, Arkansas	30 (1 year avg.)	2002 - 2003	Hoh and Hites, 2005
Cocdrie, Louisiana	16 (1 year avg.)	2002 - 2003	Hoh and Hites, 2005
California (average of six sites)	53 (BDE-47 only) 52 (BDE-99 only) 23 (BDE-209 only)	2004	Cal/EPA, 2006

Hoh and Hites (2005) measured levels of PBDEs in the atmosphere at five sites in the east central U.S. during 2002-2003. Sites were located at the Sleeping Bear Dunes National Lakeshore in Michigan; Chicago, Illinois; Bloomington, Indiana; Rohwer, Arkansas; and Cocodrie, Louisiana. The sites in Michigan and Illinois were the same location as those for work done by Strandberg et al., (2001). The mean concentration of total PBDEs was the highest at the Chicago site (100 pg/m^3), and was 3-6 times higher than at the other sites. The levels at the Chicago site were also significantly higher than measured in 1997-1999 by Strandberg et al., (2001). Deca-BDE was also measured at all sites and was found at the highest concentration at the Chicago site. Deca-BDE concentrations ranged from 2.6-956 pg/m^3 at the Chicago site, <0.02-8.3 pg/m^3 at the Michigan site, <0.02-25 pg/m^3 at the Indiana site,

<0.03 -156 pg/m^3 at the Arkansas site, and <0.03-19 pg/m^3 at the Louisiana site. Deca-BDE made up from 6% to 31% of the total PBDEs. The most abundant congener present was BDE-47, and the combination of BDE-47, BDE-99, BDE-100, and Deca-BDE composed approximately 80% of the total PBDE concentration at all sites.

Ambient air levels of PBDEs were measured at six sites in California during 2004, including Los Angeles, Oakland, Richmond, Riverside, San Jose, and Wilmington (Cal/EPA, 2006). Integrated monthly samples for three PBDE congeners were collected at each site. BDE-47 levels ranged from 7-170 pg/m^3, with an average concentration of 53 pg/m^3; BDE-99 levels ranged from 3-332 pg/m^3, with an average concentration of 52 pg/m^3, and Deca-BDE ranged from 7-72 pg/m^3, with an average concentration of 23 pg/m^3.

Levels of PBDEs measured at a rural site in southern Ontario in the year 2000, ranged from 88-1250 pg/m^3 prior to spring bud burst, and 10-230 pg/m^3 after bud burst. The highest levels were thought to be due to release from snow pack during spring melt. The major congeners found were BDE-17, BDE-28, and BDE-47 (Hale et al., 2003). Subsequent monitoring at this same location from January-June 2002, showed significantly lower levels of PBDE in the ambient air (Gouin et al., 2005). Gas phase concentrations were below the detection limit during the winter and rose to 19 pg/m^3 in early spring, and they decreased again following bud burst. The predominant congeners found were BDE-28, BDE-47, and BDE-99, with BDE-47 contributing approximately 50% of the total. The total PBDE concentration in the particulate phase ranged from below the detection limit to 34 pg/m^3, and consisted primarily of BDE-47, BDE-99, BDE-100, BDE-153, and BDE-154, with BDE-99 typically contributing 50%. The authors suggest that some local unidentified source may have been responsible for the higher levels observed in 2000 at this site, and was no longer active in 2002.

Levels of PBDEs from archived air samples from Alert, Canada in the Arctic taken between January 1994-January 1995, ranged from 1-4 pg/m^3 most of the year, but reached up to 28 pg/m^3 in July (de Wit, 2002).

Harner et al., (2006), measured PBDEs using passive air samplers at seven sites along an urban rural transect extending approximately 75 km north of downtown Toronto. Samples were collected for three consecutive seasons during 2000-2001. Total PBDEs ranged from 3-30 pg/m^3 for season averages. Air concentrations in Toronto were a factor or two greater than the rural concentrations. Lower concentrations were observed in the winter and were attributed to reduced input from indoor sources and/or more PBDEs in the particle phase during winter, which is not sampled by the passive samplers.

Shoeib (2004), reported on PBDE concentrations measured in ten indoor and three outdoor samples taken in Canada between November-December 2001, or January-March 2003. Outdoor concentrations ranged from 39-48 pg/m3.

PBDEs were measured at seven outdoor sites in Ottawa, Canada between December 2002 and March 2003 (Wilford et al., 2004a; Wilford et al., 2004b). Passive air samplers collected an air volume of approximately 250 m^3 over 72 days. Total PBDE levels ranged from <0.1-4.4 pg/m3, with mean and median values of 2.2 pg/m^3 and 2.6 pg/m^3, respectively. Only five congeners were reported to have been found at levels above the detection limit. These included BDE-17, BDE-28, BDE-47, BDE-100, and BDE-99 (Wilford et al., 2004b). The authors suggest the low level of PBDEs found in this study compared to other urban areas where higher concentrations have been observed, may be due to the restriction of the sampling period to the winter months when low temperatures result in a smaller proportion of PBDEs in the gas phase.

Atmospheric concentrations of PBDEs were measured at a municipal solid waste (MSW) incineration plant with electronic recycling and at an industrial urban reference site producing asphalt and concrete in Sweden (Agrell et al., 2004). Particle phase concentrations of total PBDEs, BDE-47, and Deca-BDE were significantly higher at the MSW plant compared to the urban reference site. For the gaseous phase, only total PBDEs and BDE-47 were significantly higher at the MSW plant.

Indoor concentration of PBDEs ranged from 15-830,000 pg/m^3 (mostly Deca-BDE) at an electronic recycling facility in California (Cal/EPA, 2006). Outdoor concentrations collected upwind and downwind of the facility ranged from 1-11,000 pg/m^3, also mostly Deca-BDE. Outdoor air concentrations of PBDEs measured upwind and downwind from an automobile shredding facility ranged from 0.2-1900 pg/m^3, mostly Deca-BDE.

Indoor Air and Dust

Indoor air and dust were sampled in 120 homes in the Cape Cod, Massachusetts area and analyzed for 89 organic compounds, including PBDEs (Rudel et al., 2003). Samples were collected during the time period of June 1999-September 2001. The authors reported that they targeted Tetra- and Penta-PBDEs for analysis, although a complete list of congeners that were analyzed was not given in the paper. No PBDEs were detected in indoor air, however three congeners were found in dust samples. BDE-99 was found in 55% of the dust samples, with a reported range of less than the reporting limit (RL) up to 22,500 ng/g, and a median value of 304 ng/g. BDE-47 was found the next most frequently (45% of dust samples) with a range of <RL to 9,860 ng/g, and a median of <RL. BDE-100 was detected in 20% of the dust samples with a range of <RL to 3,400 ng/g.

Shoeib et al., (2004), reported on PBDE concentrations measured in ten indoor and three outdoor samples taken in Canada between November-December 2001 or January-March 2003. Mean indoor air concentrations of total PBDEs ranged from 76-2088 pg/m^3. Outdoor concentrations ranged from 39-48 pg/m^3. The mean indoor/outdoor ratio for PBDEs was reported to be about 15.

PBDEs were measured in indoor air and dust samples in 74 randomly selected homes in Ottawa, Canada between December 2002 and March 2003 (Wilford et al., 2004a; Wilford et al., 2004b). Passive air samplers collected an air volume of approximately 50 m^3 over 21 days. Dust samples were collected from family vacuum cleaners of the same houses with indoor air sampling. Outdoor air samples were also taken as part of this study (see previous section of report). PBDEs were detected in all indoor air samples, with total PBDE levels ranging from 2-3600 pg/m^3, and a mean and median value of 260 pg/m^3 and 100 pg/m^3, respectively. Data was provided only for those congeners found at levels above the detection limit. This included ten PBDE congeners ranging from BDE-17 to BDE-153. The congener found at the highest concentration was BDE-47, with a range of less than the detection limit to 1600 pg/m^3, and mean and median values of 160 pg/m^3 and 66 pg/m^3, respectively. Median values of BDE-99, BDE-28, BDE-17, and BDE-100 were 15 pg/m^3, 11 pg/m^3, 6.1 pg/m^3, and 4.2 pg/m^3, respectively (Wilford et al, 2004b). Indoor PBDE concentrations were approximately 50 times higher than outdoor air concentrations. Vacuum bag dust samples taken from 68 of the 74 homes sampled for indoor air levels of PBDEs were also analyzed for PBDEs (Wilford et al., 2005). Total PBDE concentrations in dust ranged from 170-170,000 ng/g dry weight, with a median concentration of 1800 ng/g and a mean concentration of 5,500 ng/g. Deca-BDE

concentrations in dust ranged from 74-10,000 ng/g dry weight, with a median concentration of 630 ng/g, and a mean concentration of 1100 ng/g.

Dust samples collected from 16 homes in the Washington, District of Columbia area and one home in Charleston, South Carolina, between January and March 2004, were analyzed for 22 PBDE congeners (Stapleton, et al., 2004c, 2005). Clothes dryer lint was also collected from five of the 17 homes and analyzed for PBDEs. The mean and median concentration of total PBDEs in the house dust was 5900 and 4250 ng/g dry mass, respectively. Of the individual congeners, Deca-BDE was found at the highest concentrations (mean = 2090 ng/g and median = 1350 ng/g dry mass). Levels of Deca-BDE in the house dust were highly variable and ranged from 162-8750 ng/g dry mass. BDE-99 and BDE-47 were the congeners found at the next highest concentration with mean values of 1700 ng/g and1220 ng/g, and median values of 676 ng/g and 644 ng/g, respectively. PBDE levels were not correlated with the year of house construction, type of flooring (hardwood vs carpet), or the number of television sets or personal computers in the home. However, the area of the home and contribution of Deca-BDE to the total PBDE concentration in house dust was inversely correlated. Using a dust intake value of 0.02-0.2 g per day for young children and a mean value of 5900 ng/g total PBDEs, the authors estimated daily ingestion of 120-1200 ng PBDEs for this group. Using the maximum measured value of PBDEs (30,100 ng/g), the authors estimated intake of PBDEs could be as high as 6000 ng/day. Clothes dryer lint concentrations of total PBDEs ranged from 480-3080 ng/g dry mass for the five samples.

Particulate matter from vacuum cleaner bags collected from ten households in Germany and ten in Atlanta, Georgia was analyzed for various PBDE congeners (Sjodin et al., 2004). Significantly higher levels of PBDEs were found in the dust collected in the Atlanta samples compared to those from Germany. The concentration of BDE-47 in the Atlanta samples ranged from 230-3,000 ng/g dust with a median value of 430 ng/g dust, compared to a range of <14-22 ng/g and a median of <14 ng/g in the samples from Germany. Deca-BDE levels in the Atlanta samples ranged from 120-21,000 ng/g dust, with a median of 2,000 ng/g dust, compared to a range of <5-410 ng/g and a median of 60 ng/g for the samples from Germany.

Dust samples taken from the vacuum cleaners used in ten homes, representing nine different states in the U.S., were analyzed for 13 PBDE congeners (Sharp and Lunder, 2004). The household dust sampled in this study included ten of the 20 participants from a previous breast milk study on PBDEs (Lunder, 2003a). Total PBDE levels in 9 of the 10 samples ranged from 614-16,366 ng/g, with an average concentration of 4629 ng/g. One sample was treated separately because the vacuum cleaner had been used to clean up polyurethane foam residues from carpet padding, mattress pads, and an uncovered foam cushion. This sample contained 41,203 ng/g of PBDEs. BDE-47, BDE-99, and Deca-209 comprised 90% of the makeup by weight of the total PBDEs in the dust samples, with Deca-BDE the most abundant congener at 42% of the total PBDEs. Deca-BDE levels ranged from <400 ng/g-7510 ng/g, with an average concentration of 2,394 ng/g. No relationship was found between dust levels of PBDEs in the home and breast milk concentrations, as measured in the previous study.

A total of 70 dust samples from vacuum bags used in ten homes in each of seven states, including California, Maine, Massachusetts, Michigan, New York, Oregon, and Washington were analyzed for seven PBDE congeners (Costner et al., 2005). The dust samples were collected from September-October 2004. Composite samples were prepared by state, with each sample prepared from the ten designated bag samples taken from that state. Total PBDE levels ranged from 3,600-12,500 ng/g. Deca-BDE was found at the highest mean concentration, (range 901-10,000 ng/g; mean 4,660 ng/g), followed by BDE-47 (mean 2,100 ng/g), and BDE-99 (mean

1,700 ng/g). These three congeners accounted for 95% of the total concentration of PBDEs in the dust. Other congeners measured included: BDE-100, BDE-153, BDE-154, and BDE-183.

Four computer wipe samples, two from the interior of monitors and two from the PC, as well as nine vacuum bag samples were analyzed for 13 PBDE congeners. The dust samples came from homes, and the computer samples from offices located in Dallas, Texas (Schecter, et al., 2005b). Total PBDEs in the computer wipe samples ranged from 77-1536 ng/100cm^2. Deca-BDE was the predominant congener (53.2%-95.2% of total PBDEs) in all samples, with concentrations ranging from 73.3-821 ng/100cm^2. In the dust samples, total PBDEs ranged from 705-69,283 ng/g dry weight, with a median concentration of 2507 ng/g and mean concentration of 12,136 ng/g. Deca-BDE dust concentrations ranged from 536-65,777 ng/g, with a median concentration of 665 ng/g and a mean concentration of 8567 ng/g. Table 14 provides a summary of total PBDE levels in house dust from the various studies.

Table 14: Total PBDE Concentrations in Indoor House Dust Samples

Location	Number of Samples	Year	Range (ng/g)	Median (ng/g)	Mean (ng/g)	Reference
Ottawa, Canada	68	2002-2003	170 – 170,000	1,800	5,500	Wilford et al., 2005
Washington, D.C.	16	2004	780 – 30,100	4,250	5,900	Stapleton, et al., 2004c, 2005
9 United States states	10	2003	614 – 41,203	3,181	4,629 (n = 9)	Sharp and Lunder, 2004
7 United States states	7 composite (from 70 individual)	2004	3,600 – 12,500	N.A.	8,900	Costner et al., 2005
Dallas, TX	9	N.A.	705 – 69,283	2,507	12,136	Schecter et al., 2005b

N.A. = Not available

Organic films were collected from the indoor and outdoor surfaces of windows and analyzed for 41 PBDE congeners (Butt et al., 2004). Samples were collected from the windows of buildings located along an urban rural transect extending from downtown Toronto, Ontario, approximately 80 kilometers (km), northward. The samples were taken from July to early August, 2001, at nine sites, including seven in downtown Toronto, one in a suburban area north of Toronto, and the other a rural site located 80 km north of Toronto. The urban sites had higher concentrations of PBDEs than rural site for both indoor and outdoor films. Total PBDEs in exterior films ranged from 2.5-14.5 ng/m^2 at urban sites, compared to 1.1 ng/m^2 at the suburban site, and 0.56 ng/m^2 at the rural site. Total PBDE in interior films ranged from 19.4-75.9 ng/m^2 at the urban sites, compared to 10.3 ng/m^2 at the rural site. Total PBDE levels at an electronics recycling facility in Toronto (not included in the urban site analysis) were 38.7 and 755 ng/m^2 for exterior and interior films, respectively. These levels were about 4.4 and 22 times higher than the other urban samples in Toronto, and were indicative of a “hotspot”. Congener profiles were

considered similar among all samples with Deca-BDE found in the highest amount. Geometric means of the six main congeners calculated as a percent of the total mass were as follows: Deca-BDE, 51.1%; BDE-99, 13.6%; BDE-47, 9.4%; BDE-100, 2.3%; BDE-153, 1.7%; BDE-183, 1.5%.

Gearhart and Posselt (2005), found significantly higher concentrations of PBDEs on the interior surface of automobile windows, compared to the interior surface of windows of buildings found by Butts et al., (2004). Windshield wipe samples were collected from 111 vehicles that visited a local household recycling center in Michigan. Composite samples consisting of wipes from 6-10 vehicles for 11 different automobile manufacturers were analyzed for PBDEs. Model years for the automobiles ranged from 2000-2005, and vehicles which had windows cleaned within the last two weeks were not sampled. In the windshield film, mean concentrations of PBDE-99 were found at the highest level (158 ng/m^2), followed by PBDE-47 (65 ng/m^2), PBDE-100 (53 ng/m^2), PBDE-153 (41 ng/m^2), and PBDE-154 (32 ng/m^2), while Deca-BDE was found only at 6 ng/m^2. Total mean concentration of PBDEs was 365 ng/m^2. Two dust composite samples, consisting of dust collected from 22 vehicles were also analyzed for PBDEs. In contrast to the windshield films, Deca-BDE was found at the highest mean concentration (9,500 ng/g), and the next two highest congeners were BDE-47 (600 ng/g) and BDE-99 (600 ng/g). The total mean PBDE concentration in the dust was 10,950 ng/g.

Water

Very little monitoring data are available for PBDEs in surface waters in North America. PBDE levels measured in the Lake Michigan water column in 1997-1999 ranged from 31-158 pg/L. Concentrations measured in Lake Ontario were lower and reported at 6 pg/L (Hale et al., 2003). The concentration of total PBDEs in five samples collected from Lake St. Clair, Michigan in 2005, ranged from 330-23,210 pg/L (MDCH, 2006).

Water samples were taken from the San Francisco Estuary in July 2002, at 28 spatially randomized and five fixed nonrandomized sampling stations, and analyzed for 22 PBDE congeners (Oros et al., 2005). The total PBDEs in the water samples ranged from 3-513 pg/l. BDE-47, BDE-99, and Deca-BDE were the most abundant congeners found in the water samples. Deca-BDE concentrations ranged from below the detection limit up to 191 pg/L. The highest total PBDE levels were concentrated around an area that receives 26% of the Estuary's total publicly owned treatment works wastewater effluents and about 10% of the Estuary's freshwater inflow.

Sediment and Soil

Sediments from freshwater tributaries in Virginia were analyzed for PBDEs. PBDEs were detected (>0.5 µg/kg dw) in 22% of surficial sediment samples taken from 133 sites. BDE-47 was the dominant congener found, followed by BDE-99, and BDE-100. The maximum concentration was 52.3 µg/kg. Sediment taken from a stream in North Carolina near a recently closed polyurethane foam manufacturing facility had up to 132 µg/kg Penta-DBE. The soil outside the facility had 76 µg/kg (Hale et al., 2003).

Deca-BDE was the major congener detected in surficial sediment samples taken from Hadley Lake in Indiana near a research and development facility of a PBDE producer. Other congeners detected included BDE-99, BDE-153, BDE-154, BDE-47, and BDE-100. Concentrations of Deca-BDE ranged from 19-36 µg/kg, and all other congeners were less than 5 µg/kg. (Hale et al., 2003).

Sediment samples taken in 2001 and 2002 from six locations in Lake Superior were analyzed for ten PBDE congeners (Song et al., 2004). Deca-BDE was found at the highest concentration. The concentration of total PBDEs (excluding Deca-BDE) in surficial sediments ranged from 0.49-3.1 ng/g dw, with an average of 1.4 ng/g dw. The concentration of Deca-BDE in surficial sediment ranged from 4.3-17.5 ng/g dw. The surface concentration and flux of Deca-BDE ranged from 79%-98% of the total PBDEs on a mass basis. Calculated fluxes from the sediment data showed continuous increases since the 1970s when PBDE commercial production began. Current fluxes for total PBDEs (excluding Deca-BDE) ranged from 8-31 pg/cm2/yr. Based on this range, the current loading of total PBDEs to Lake Superior sediments is at a rate of 7-25 kg/yr, and if Deca-BDE is included, it is 80-160 kg/yr.

Sediment cores taken from three locations in Lake Michigan and from three locations in Lake Huron in 2002, were analyzed for nine PBDE congeners (Tri- to Hepta-BDE) and Deca-BDE (Song et al., 2005a). The total PBDEs in the surficial sediments of Lake Michigan for the tri- to hepta-BDEs ranged from 1.7-4.0 ng/g dry weight, compared to 43.9-95.6 ng/g dry weight for Deca-BDE. In Lake Huron, total PBDEs in the surficial sediments for the tri- to hepta-BDEs ranged from 1.0-1.9 ng/g dry weight, compared to 8.6-25.1 ng/g dry weight for Deca-BDE. Deca-BDE is the congener present at the highest concentration in both lakes, and was found to be about 96% of the total PBDEs on a mass basis in Lake Michigan, and 91% in Lake Huron. The flux to the sediment of the Tri- to Hepta-BDEs ranged from 36-109 pg/cm^2/year for Lake Michigan, and from 30-73 pg/cm^2/year for Lake Huron. Deca-BDE fluxes ranged from 0.64-2.04 ng/cm^2/year for Lake Michigan and 0.67-1.41 ng/cm^2/year for Lake Huron. PBDE concentrations and fluxes increased upward toward the sediment surface and present time. Estimated doubling times for PBDEs in sediments of Lake Michigan ranged from 10-13 years, and in Lake Huron from 10-12 years, with the exception of one sample location, where the doubling time was estimated to be approximately 20 years.

Song et al., (2005b), analyzed sediment cores for nine PBDE congeners (Tri- to Hepta-BDE) and Deca-BDE. Samples were taken in 2002 from two locations each in Lake Ontario and Lake Erie. Zhu and Hites (2005) analyzed sediment core samples taken from a single location in Lake Huron and Lake Michigan in 2004. Results for Deca-BDE from these two studies, along with other Great Lakes sediment data are shown in Table 15.

Table 15: Deca-BDE in the Sediments of the Great Lakes

Lake Sampling Site	Year	Surficial Concentration (ng/g)	Inventory (ng/cm^2)	Surface Flux (ng/cm^2/year)	Reference
Michigan 18	2002	49.9	82	0.64	Song et al., 2005a
Michigan 41	2002	43.9	48.6	1.2	Song et al., 2005a
Michigan 47	2002	95.6	68.5	2.04	Song et al., 2005a
Michigan 47	2004	63	38	0.98	Zhu & Hites, 2005
Huron 12	2002	36	25.1	1.41	Song et al., 2005a
Huron 38	2002	21.5	14	0.67	Song et al., 2005a
Huron 48	2002	28.8	8.64	0.86	Song et al., 2005a
Erie 9	2002	55.4	76.2	8.93	Song et al., 2005b
Erie 37	2002	50.2	68	3.71	Song et al., 2005b
Erie 15	2003	39	40	3.6	Zhu & Hites, 2005
Ontario 30	2002	211.2	86.7	6.5	Song et al., 2005b
Ontario 40	2002	242	140.8	7.33	Song et al., 2005b
Superior (avg)	2001-2002	11	4.8	0.14	Song et al., 2004

Six sediment samples were collected from Lake St. Clair, Michigan in 2005 (MDCH, 2006). These samples were collected from sites known to be contaminated with metals, pesticides, and/or other substances. At least one PBDE congener was detected in five of the six samples. The congener, Deca-BDE, was found at the highest concentration and was present at concentrations ranging from 25 to 160 ng/g. Congeners BDE-99 and BDE-47 were also present in some of the samples at concentrations >1 ng/g. The concentration of total PBDEs ranged from 25-163 ng/g in the five samples with detectable levels of PBDEs.

The MDEQ in 2006 analyzed surficial (ponar) and core sediment samples collected in 2004 from 29 locations in the Shiawassee River, 21 locations in the Saginaw River, and five locations in the Saginaw Bay. Results for the sum of nine Tri- through Hexa- substituted PBDEs, BDE-203, and Deca-BDE in surficial sediments from this study are shown in Table 16. Floodplain soil samples were also collected as part of this study and are shown in Table 17.

Table 16: PBDE Concentrations for Sediments from the Saginaw Bay Watershed (MDEQ, 2006)

Summary Statistics	Shiawassee River Sediments			Saginaw River Sediments			Saginaw Bay Sediments		
	Σ of 9 PBDEs	BDE-209	BDE-203	Σ of 9 PBDEs	BDE-209	BDE-203	Σ of 9 PBDEs	BDE-209	BDE-203
	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)
Average (Mean)	0.50	2.3	0.65	0.40	3.5	0.31	0.37	3.6	13
Median	0.31	1.5	0.090	0.14	1.0	0.0000	0.13	1.6	0.0000
Standard Deviation	0.70	2.7	2.0	0.58	8.4	0.58	0.4	4.8	51
Min	0.017	0.11	<0.04	0.002	0.04	<0.04	0.0059	<0.04	<0.04
Max	3.6	13	11	2.5	48	2.1	1	16	200
N	32	32	32	35	35	35	15	15	15
# of n.d.	0	0	11	1	0	20	0	2	10

Table 17: PBDE Concentrations for Floodplain Soils from the Saginaw Bay Watershed (MDEQ, 2006)

Summary Statistics	Shiawassee River All Floodplain Soils			Saginaw River All Floodplain Soils			Saginaw Bay All Floodplain Soils		
	Σ of 9 PBDEs	BDE-209	BDE-203	Σ of 9 PBDEs	BDE-209	BDE-203	Σ of 9 PBDEs	BDE-209	BDE-203
	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)	(ng/g)
Average (Mean)	3.5	11	2.2	0.30	2.6	0.11	0.28	0.59	0.16
Median	1.1	7.1	0.66	0.12	0.28	0.017	0.21	0.42	0.00
Standard Deviation	4.8	12	4.1	0.43	5.2	0.19	0.32	0.80	0.25
Min	0.21	0.60	0.056	0.03	<0.04	<0.04	0.020	<0.04	<0.04
Max	15	41	14	1.5	19	0.62	0.83	2.2	0.54
N	10	10	10	14	14	14	6	6	6
# n.d.s	0	0	0	0	1	7	0	2	4

The MDEQ (2006), found PBDEs in all floodplain soil and sediment samples. Deca-BDE was the predominant congener in floodplain soils and sediments. There did not appear to be a consistent concentration or distribution pattern for BDE-203 or Deca-BDE congeners. The other nine Tri-Hexa PBDE congeners appeared to have a consistent congener distribution pattern in all floodplain soils and in the Shiawassee and most of the Saginaw River sediments. This

congener distribution changes with BDE-28 being a more predominant component for some sediment samples in the Saginaw River and the sediment samples from Saginaw Bay. The concentrations of the sum of nine Tri-Hexa PBDEs and Deca-BDE in surficial sediments from this study were lower than those reported for other locations in the Great Lakes surficial sediments as shown in Table 18.

Table 18: Comparison of Surficial Sediments from the Great Lakes and Tributaries

Water Body -	Year	Tri-Hepta Surficial Concentration (ng/g)		BDE 209 Surficial Concentration (ng/g)		n =	Reference
		average	median	average	median		
Michigan	2002-2004	2.9	3.0	63	56	4	Song et al., 2005a; Zhu & Hites, 2005
Huron	2002	1.5	1.7	29	29	3	Song et al., 2005a
Erie	2002-2003	1.6	1.8	48	50	3	Song et al., 2005b; Zhu & Hites, 2005
Ontario	2002	5.6	5.6	227	227	2	Song et al., 2005b
Superior	2001-2002	1.4	1.1	11	9.6	6	Song et al., 2004
Saginaw Bay	2004	0.34	0.065	2	0.13	5	MDEQ, 2006
Saginaw River	2004	0.60	0.38	5.1	1.3	21	MDEQ, 2006
Shiawassee River	2004	0.55	0.33	2.3	1.1	29	MDEQ, 2006

Sediment samples taken from the San Francisco Estuary in July 2002 were analyzed for 22 PBDE congeners (Oros et al., 2005). The total PBDEs in the samples ranged from below detection limits to 212 ng/g dry weight. Only five PBDE congeners were detected in the sediment samples, with BDE-47 the most abundant, followed by BDE-99. BDE-183, BDE-204, and BDE-205 were only found in one or two of the 48 samples. The range of PBDE concentrations found in the sediment samples are shown in Table 19.

Table 19: Range of PBDE Concentrations in Sediment Samples from San Francisco Estuary (Oros et al., 2005)

PBDE Congener	Concentration (ng/g dry weight)
BDE-47	<0.5 – 100
BDE-99	<0.2 – 71
BDE-183	<0.1 – 0.2
BDE-204	<0.5 - 19
BDE-205	<0.5 - 22

Samara et al., (2006), analyzed sediment samples taken from 11 sites in the Niagara River during May 2003, for nine PBDE congeners (not including Deca-BDE). Total PBDE concentrations ranged from not-detected to 148 ng/g. The highest concentrations were reported to be found in sediments collected from sites closest to the discharge locations of municipal wastewater treatment plants and local industries.

Hites (2004a), analysis of sediment data, indicates Deca-BDE is often present in this media, even though not abundant in other environmental samples, including biota.

Sewage Sludge

Concentrations of PBDEs in 11 sludge samples collected from four different regions in the United States ranged from 1,100-2,290 µg/kg dw basis. These concentrations represent the sum of BDE-47, BDE-99, BDE-100, BDE-153, and BDE-154, and were similar between samples, regardless of location. The concentrations of Deca-BDE, however, varied substantially between samples with a range of 84.8-4,890 µg/kg (Hale et al., 2003).

Sewage sludge samples from communities in the Lake Superior and Lake Michigan watersheds were analyzed for several PBDE congeners (Hale et al., 2003). Results are shown in Table 20.

Table 20: PBDE Concentrations in Sewage Sludge (Hale et al., 2003)

PBDE Congener	Sludge Concentration (ug/kg)	
	Lake Superior Communities	Lake Michigan Communities
BDE-47	767	507
BDE-99	1,327	706
BDE-209	510	466

Sludge and treated effluent samples collected from the wastewater treatment plant in Palo Alto, California, over a three day period, were analyzed for 41 PBDE congeners (North, 2004). BDE-47, BDE-99, and BDE-209 comprised about 85% of the total PBDEs in the sludge with mean concentrations of 757, 944, and 1183 µg/kg dw, respectively. The mean concentration of the total PBDEs in sludge was 3381 µg/kg dw. BDE-47 and BDE-99 were present at the highest concentrations in the effluent, with mean concentrations of 10,467 and 11,200 pg/L, respectively. The mean concentration of Deca-BDE in the effluent was 1730 pg/L, followed by BDE-153 at 983 pg/L, and BDE-154 at 776 pg/L. These five congeners comprised about 90% of the total PBDEs (mean = 29,023 pg/L) in the effluent.

PBDE concentrations in sewage sludge samples from North America are substantially higher than found in Europe. In Sweden and Germany in the late 1980s, concentrations ranged from 0.4-30 µg/kg. More recent data have shown higher levels with an average concentration of 162 µg/kg total PBDEs from eight German plants. In more recent data from Sweden, the total concentration of BDE-47, BDE-99, and BDE-100 ranged from 105-205 µg/kg, while levels of BDE were 170-270 µg/kg (Hale et al., 2003).

POTENTIAL RISKS

The Potential Risk section of the 2004 Draft PBDE Background Paper was very brief and did not include a quantitative risk assessment, due to the limited data available at the time; it can be found in Appendix B. The following updated discussion presents a quantitative risk assessment using a MOE approach. Assessing the potential human health risks from PBDEs poses several challenges. It would be best to utilize epidemiology studies that have evaluated all potential effects in humans for any PBDE risk assessment. Although there are some data on human exposures, sufficient human data which directly evaluate adverse effects associated with those exposures are not available at this time. Lacking human data, toxicological data in animals may be used to assess the risks of PBDEs to humans; however, uncertainties arise since it is not known if humans respond in the same manner as the laboratory animals. Other challenges include determining dose equivalencies between humans and animals. Considering these difficulties and uncertainties, various approaches for assessing risks from PBDEs have been used. The methodologies and findings of three different approaches are identified and summarized below:

1) A risk assessment for children exposed to Deca-BDE by Hays and Pratt (2006);

2) A risk assessment for total PBDEs by McDonald (2005), and

3) A risk assessment of BDE-47, BDE-99, BDE-153, and total PBDEs by the MDEQ's TSG in this report.

Each of these three assessments uses either a hazard quotient (HQ) or a MOE approach to estimate the potential risks from exposure to PBDEs. A HQ is the ratio of the exposure dose to an estimated safe dose in humans. The HQ cannot be translated to a probability that adverse health effects will occur and is unlikely to be proportional to risk. A HQ value of less than one indicates that adverse effects are not likely to occur, and thus the risk is considered negligible. Values greater than one indicate that exposure concentrations exceed the estimated safe dose in humans, and as a result, the risk may be significant. The MOE approach is similar to the HQ approach, except the ratio is reversed and uncertainty/variability are not considered in the calculated value. The MOE is the ratio of either an adverse effect level or a no-adverse effect level to the exposure dose. The MOEs based on effect levels do not quantitatively account for uncertainties as the HQ approach does. This is based on the fact that the HQ approach uses acceptable doses, which are derived via the application of UFs, while MOEs based on effect levels do not incorporate UFs. As a result, consideration of the potential uncertainty is imperative in evaluating a MOE.

All three of the above approaches use animal toxicity data to assess risks to humans. Comparison of target tissue levels in humans to target tissue levels causing adverse health effects in experimental animals is preferred. Target tissue levels are concentrations of a contaminant in the specific organ or tissue where the critical toxic effect occurs. Unfortunately, target tissue levels for both animals and humans are not currently available. The next best

approach is to compare tissue levels that represent body burdens. Estimates of animal body burdens can be calculated from administered doses for comparison with reported human body burdens. The McDonald (2005) and the MDEQ TSG risk assessments use this body burden approach. In contrast, Hays and Pyatt (2006), estimate human intake levels from various exposure routes.

Assessment of Deca-BDE Exposures to Children by Hays and Pyatt (2006)

Hays and Pyatt (2006) used a HQ approach to estimate the risks associated with children's exposure to Deca-BDE. Risks were determined for children (>2-18 years old) exposed to Deca-BDE via contaminated soil, dust, air, and food. Risks were also determined for infants (0-2 years old) whose mothers were involved in either the formulation of Deca-BDE or the disassembly of products containing Deca-BDE. Infants were considered to be potentially exposed to Deca-BDE via the ingestion of breast milk, the inhalation of particulates, and the mouthing of fabrics and electronics containing Deca-BDE. Mid-range and upper-end estimates of intakes were determined for all of the exposure pathways. A HQ was derived by dividing the total exposure for each of the three receptor populations by the RfD of 4 mg/kg/d derived by the National Academy of Science (NAS, 2000). The HQs for the mid-range estimates ranged from 0.0003-0.01, whereas, the HQs for the upper estimates ranged from 0.1 to 0.2. Based on these results, the researchers concluded that the current levels of Deca-BDE in the United States are unlikely to represent an adverse health risk to children.

Assessment of Total PBDEs by McDonald (2005)

McDonald (2005) estimated the distribution and variability of total PBDE concentrations in serum, adipose tissue, and breast milk among women residing in the U.S. The tissue concentrations in humans were then compared to the estimated and measured tissue concentrations associated with developmental neurotoxicity and reproductive effects in rodents. The PBDE levels reported in six groups of U.S. women were utilized for this study. Several developmental neurotoxicity and developmental reproductive rodent studies were used to identify no-effect levels and from these, lipid-normalized concentrations in rodent tissues (C_{rodent}) were estimated and compared to lipid-normalized PBDE concentrations in humans (C_{human}). The ratio of C_{rodent} to C_{human} was identified as a measure of the MOE.

Wide variability (about 50-fold) was seen in PBDE levels in serum, breast milk, and fat of individual women. Distributions in the three media were similar so data from all media were combined. The median and mean concentrations for all media combined are 47.9 and 90.3 ng/g lipid, respectively. The upper 95th percentile of the combined distribution is 302 ng/g lipids. This level was the basis for comparisons with rodent tissue levels. Twelve out of 191 (6.3%) women sampled had lipid normalized total PBDE levels greater than 300 ng/g.

McDonald utilized 14 rodent studies for the generation of rodent tissue concentrations (C_{rodent}) and their comparison to human tissue concentrations (C_{human}). The C_{rodent} to C_{human} ratios or MOEs ranged from <1 to 36,000. Some of the reported rodent tissue concentrations were based on LOELs, and some were based on NOELs. To convert the LOEL-based C_{rodent} values to NOEL-based values, the C_{rodent} concentrations are reduced by a factor of ten. The studies that yielded some of the lowest MOEs were studies reporting behavioral alterations in mice using PBDE-47, -99, or -153; the MOEs were 11, four, and six, respectively. Studies using PBDE-99 and investigating the effects of early life exposure on the development of reproductive

systems in male and female rats yielded rodent tissue concentrations that are the same as the concentrations currently seen in humans (based on LOELs rather than NOELs).

McDonald also provided an estimate of the total daily intake of the five predominant PBDE congeners among U.S. women from tissue concentrations and estimates of terminal half-lives in humans. The mean intake derived from the body burden data is 16 ng/kg/d, with an upper 95th percentile estimate of 53.6 ng/kg/d.

Assessment of BDE-47, BDE-99, BDE-153, and Total PBDEs by the MDEQ TSG

The TSG PBDE Subcommittee compared congener-specific human body burdens to estimated animal body burdens for specific congeners not including Deca-BDE (Deca-BDE). A quantitative risk assessment was included for Deca-BDE in the 2007 version of the PBDE report; however, it was withdrawn from this version when additional data were published providing more support that Deca-BDE behaves differently *in vivo* than the lower brominated congeners and is distributed widely throughout the body, i.e. not primarily to lipids. In addition, new data also provide further support for the *in vivo* metabolism of Deca-BDE, including metabolism to lower brominated congeners. It is not known at this time if the risk assessment should be based on the parent compound (Deca-BDE) and/or its metabolites. Considering these new data, the methodology used in the 2007 report does not seem appropriate for Deca-BDE and raises significant uncertainty regarding alternative risk assessment methodologies. More detailed information regarding the metabolism, distribution, and elimination of Deca-BDE and a better understanding of the ultimate toxicant(s) is needed before a quantitative risk assessment with an acceptable level of uncertainty can be conducted.

Estimates of animal body burdens for the lower brominated PBDE congeners were calculated from LOAELs reported in several animal toxicity studies reviewed and summarized in this report. The basis of the animal body burdens were the lowest LOAELs for each of the following PBDE congeners: BDE-47, -99, and -153. These LOAELs were reported as intake doses in units of mg/kg from the animal studies. To estimate body burden LOAELs (ng/g lipid), it was assumed that the total absorbed dose partitioned equally into the lipid compartment of the body. Parameters used in the calculation included the congener-specific LOAEL (mg/kg), an assumed fraction of the BDE absorbed (unitless), and an assumed fraction of body weight as lipid (unitless), as shown below (see Table 21 for specific values used). The calculation of the estimated body burdens does not consider elimination from the body and is therefore likely to be an overestimation of the animal body burdens.

Table 21: TSG Determinations of MOEs for Human PBDE Tissue Levels Based on Animal Toxicity Data

PBDE	Study	Effect	Animal Model Species, Gender, Age	LOAEL Dose (mg/kg)	Fraction Body Weight as Lipid (assumed)	Fraction Absorbed (assumed)	Estimated Animal Model Body Burden at LOAEL (ng/g lipid)	Human Tissue Lowest Median Value (ng/g lipid)	MOE Low Median (Estimated Body Burden LOAEL/ human tissue)	Human Tissue Highest Median Value (ng/g lipid)	MOE High Median (Estimated Body Burden LOAEL/ human tissue)	Human Tissue Highest Value (ng/g lipid)	MOE Highest Value (Estimated Body Burden LOAEL/ human tissue)
BDE-47 (Tetra-BDE)	Kuriyama et al., 2004	Increased Locomotor Activity	Wistar Rat, Female, GD6	0.7	0.07	0.75	7,500	13	600	46	200	2720	3
Reference for Value					Lopez-Luna et al., 1991	Sanders et al., 2006		Schecter et al., 2005a		Sjodin et al., 2004		Johnson-Restrepo et al., 2005	
BDE-99 (Penta-BDE)	Kuriyama et al., 2005	Increased Locomotor Activity; Male Reproductive (decrease number sperm and spermatids, epididymis weight)	Wistar Rat, Male and Female; Male, GD6	0.06	0.07	0.78	670	3	200	13	50	1380	0.5
Reference for Value					Lopez-Luna et al., 1991	McDonald, 2005; Hakk et al ., 2002		Schecter et al., 2005a		Sjodin et al., 2004		Johnson-Restrepo et al., 2005	
BDE-153 (Hexa-BDE)	Viberg et al., 2003	Activity Profile, Morris Water Maze	NMRI Mouse, Male, PND 10	0.9	0.02	0.35	16,000	2.0	8,000	10	2,000	3180	5.0
Reference for Value					Birnbaum, 2006	Hakk and Lechter, 2003		Johnson-Restrepo et al., 2005		Lunder and Sharp, 2003a		Johnson-Restrepo et al., 2005	
Total PBDEs Compared to Lowest LOAEL	Kuriyama et al., 2005	Lowest LOAEL BDE-99 Motor Activity & Male Reproductive	Wistar Rat, Male, GD6	0.06	0.07	0.78	670	25	30	77	9	9630	0.07
Total PBDEs Compared to Highest LOAEL	Viberg et al., 2003	Activity Profile, Morris Water Maze	NMRI Mouse, Male, PND 10	0.9	0.02	0.35	16,000	25	600	77	200	9630	2
Reference for Value								Ryan et al., 2002		Johnson-Restrepo et al., 2005		Johnson-Restrepo et al., 2005	

The MOEs were calculated by dividing the estimated animal body burden LOAEL by the human tissue levels. The human tissue levels used for generation of the MOEs were the lowest median body burden value, the highest median body burden value, and the highest body burden concentration from the studies reviewed for this report (see Table 21). The use of the highest body burden represents a worst case estimate based on actual data. The MOE determined from this body burden is the highest possible based on the sample data, but may not be the highest in the population of the U.S., given the limited data. Of the specific congeners, BDE-99 had the lowest MOEs and therefore, the highest risk, while BDE-153 had the highest MOEs and therefore, the lowest risk. Using the MOE based on the highest human body burden concentration from all of the studies for a specific congener, the MOEs are 3.0, 0.5, and 5.0 for BDE-47, -99, and -153, respectively.

The TSG also estimated MOEs for total PBDEs similar to the McDonald (2005) approach. Since toxicological data were not available for total PBDEs, congener-specific LOAELs were used in this assessment. In an attempt to bracket the potential risk based on total PBDEs, data from the most toxic congener (lowest LOAEL) and least toxic congener (highest LOAEL) were used to determine the MOEs for total PBDEs. The MOE using the highest human tissue level measured for total PBDEs ranged from 0.07-two. Using the highest median tissue concentration, the MOEs ranged from nine-200. The significance of these MOEs is discussed below in the section titled, “Significance of MOEs”.

The MOEs developed by the TSG have several uncertainties associated with the simplified assumptions used to estimate the animal body burden/tissue levels and the risks to humans based on the animal data. They are listed below:

Uncertainties associated with the estimates of animal body burdens at the LOAEL:

1) The distribution of PBDEs is assumed to be homogeneous in all tissues. However, it is known that distribution of the lower brominated congeners to adipose tissue is greater than their distribution to blood. For Deca-BDE, lower distribution to adipose tissue is reported compared to more highly perfused tissues (Morck et al., 2003). The use of PBDE concentrations in human adipose tissue (highest human tissue levels) may overestimate the risk, while using PBDE concentrations in blood may underestimate the risk for the lower brominated congeners.

2) The assumed absorption efficiencies were not obtained from the LOAEL study to which they are applied, but rather from a similar study. It is uncertain if this will overestimate or underestimate risk.

3) The estimated animal body burdens do not take into account any elimination of the congener or it’s potentially toxic metabolites. This may overerestimate the internal dose that results in adverse effects, thus underestimating the risk.

4) The fraction body weight, as lipid, is not derived from the LOAEL studies to which they are applied. However, for BDE-47 and BDE-99, studies similar in species and pregnancy state were used to derive the fraction body weight as lipid. This may result in an under or overestimation of risk.

Animal-to-human toxicokinetic differences should be accounted for with the uncertainties identified for the animal body burden estimates listed above. The potential for underestimating risks, due to human variability from exposure and toxicokinetics factors, should be minimized by

using maximum reported human tissue levels for comparisons with the estimated body burdens at the LOAEL.

Uncertainties in using animal data to estimate risks in humans:

1) The sensitivities of experimental animals and humans to a particular toxic effect may be different. This may result in an over or underestimation of risk.

2) The variability in response to the exposure among experimental animals and humans may be different. The risk may be underestimated for more sensitive humans.

3) The total PBDE MOE approach assumes that all PBDE congeners are equally toxic. The information currently available in the scientific literature indicates that different PBDE congeners exhibit varying levels of toxicity. Comparing human body burdens to the animal body burden estimated from the lowest LOAEL for specific congeners may overestimate the risk, while comparing to body burdens from the highest LOAEL may underestimate the risk.

Other uncertainties:

1) The individual congener-specific MOEs do not account for additivity or other chemical interactions that may occur from typical exposures to PBDEs. This may result in an over or underestimation of risk.

2) This approach does not take into account potential environmental breakdown products from the higher brominated PBDEs and the resulting exposure to the lower brominated and more toxic congeners. This may underestimate the risk for the higher brominated congeners.

3) Most of the highest human tissue values were analyzed from adipose tissue collected through liposuction. This type of tissue may not represent body burden levels available to cause adverse effects, so may overestimate the risk to human health. Even without using these adipose tissue levels, the highest human tissue level MOEs would be 16, 3, and 24 for BDE-47, -99, and -153 respectively, still well below the acceptable MOE of 300. The total PBDE MOE range would be 0.6-93, also extending well below the acceptable MOE.

Discussion and Comparison of the Three Approaches

The major advantage of the McDonald (2005) approach and the TSG approach over the Hays and Pyatt (2006) approach is the use of body burden levels as the basis for the evaluation. Using actual measured body burdens in humans eliminates the uncertainty in trying to estimate intake levels from various exposure routes such as inhalation, ingestion from food, exposure from house dust, occupational exposure, and breast milk. Measured body burden levels also minimize uncertainties regarding absorption, distribution, and elimination between species, since these processes are inherent to the body burden levels. It has been shown that PBDEs are retained longer in the human body than they are in rodents. As a result, human body burdens will be higher than those in animals receiving the same intake dose.

Another major concern with the Hays and Pyatt study is use of the RfD of 4 mg/kg/d as the toxicity benchmark for Deca-BDE. This RfD was derived by dividing the NOAEL of

1,120 mg/kg/d reported in a two year study in rats (NTP, 1986) by an UF of 300 (10x each for intraspecies and interspecies extrapolation and 3x for database uncertainty). Liver toxicity was the most sensitive effect found in this study however, liver toxicity is not the most sensitive effect for Deca-BDE. Deca-BDE has been shown to cause neurodevelopmental effects in mice exposed to a single dose of 20.1 mg/kg on PND 3 (Viberg et al., 2003a) with a much lower NOAEL of 2.22 mg/kg. Since the NTP study did not examine neurodevelopmental effects, the use of this study may underestimate risks for children. In a recent draft report, the U.S. EPA has developed a new RfD of 0.007 mg/kg-day for Deca-BDE (EPA, 2006). This draft RfD value is based upon the neurodevelopmental effects observed in the Viberg et al., (2003a) study. While still draft, the use of more recent data identifying neurodevelopmental effects as the most sensitive effect for developing an RfD provides additional support for the concern with the Hays and Pyatt study. Lastly, derivation of a HQ rather than a MOE is another concern with the Hays and Pyatt study. Comparisons based on an adverse effect level, rather than a safe or acceptable level, can be more informative regarding the likelihood of adverse effects occurring, since it eliminates the use of UFs inherent in the HQ approach. For these reasons, the results of the Hays and Pyatt study will not be considered further.

The TSG and the McDonald approaches are relatively similar. The McDonald approach compared congener-specific animal body burdens to human body burden data representing total PBDEs, whereas the TSG approach compared congener-specific animal body burdens to congener-specific human body burdens. McDonald bases animal body burden data on NOELs in some cases and on LOELs in others, whereas the TSG approach relies strictly on LOAELs. The human body burden concentrations in the McDonald study were represented by the 95th percentile of total PBDEs in all media (concentrations in serum, milk, and adipose tissue combined). The resulting MOEs ranged from <1 for BDE-99 (based on a LOEL) up to 1,300 for Penta-BDE (based on a NOEL). The MOEs generated by the TSG are based on maximum, highest median, and lowest median human body burden concentrations from any study reviewed for this report. Unlike McDonald, the TSG approach did not pool data from different studies in selecting tissue concentrations to use in the risk assessment. In comparing the TSG MOEs based on the highest human tissue values to the McDonald MOEs, the range of the TSG MOEs are 2-3.6-fold lower than the range presented by McDonald. The TSG approach, which used more recent and higher human tissue data, e.g., adipose from liposuction (Johnson-Restrepo, et al., 2005), accounts for some of the difference between the two groups of MOEs.

Significance of MOEs

There is little regulatory guidance on interpreting the significance of MOEs. In a document describing the use of the RfD in risk assessment (EPA, 1993), the U.S. EPA has stated that the need for regulatory concern is likely to be small when the MOE is equal to or greater than the total UF used in developing an RfD. If the MOE is less than the total UF, there is potential concern, and a case-by-case evaluation needs to be done with consideration given to all relevant information to make a risk management decision. Factors to consider in risk management decisions are described below:

"Once the risk characterization is completed, the focus turns to risk management. In reaching decisions, the risk manager utilizes the results of risk assessment, other technological factors, and legal, economic, and social considerations in reaching a regulatory decision. These additional factors include efficiency, timeliness, equity, administrative simplicity, consistency, public acceptability, technological feasibility, and nature of the legislative mandate."

"…after carefully considering the various risk and non-risk factors, regulatory options, and statutory mandates in a given case (i), the risk manager selects the appropriate statutory alternative for arriving at an "ample" or "adequate" margin of exposure [MOE(i)]" (EPA,1993).

The total UF that might be used in developing RfDs from the animal LOAEL data presented in Table 21 is approximately 300. This includes a ten-fold reduction to account for intraspecies variation and a three-fold reduction for interspecies variation (less than ten-fold due to the fact that the use of body burden levels may eliminate *some* of the uncertainty). In addition, an UF of ten is typically applied for converting the LOAEL to a NOAEL. This UF of 300 does not account for exposure duration. For example, in the U.S. EPA toxicological review for Deca-BDE mentioned earlier in this section (EPA, 2006) an UF of three was used to account for extrapolating from a single neurodevelopmental exposure to a lifetime exposure. If incorporated, it could change interpretation of the specific MOEs.

Considering the above information, an animal LOAEL-based MOE of 300 or greater may pose a minimal level of risk to humans based on scientific information currently available in the published literature. A value of 300 would be similar to the total UF that would be used to derive an RfD based on a LOAEL found in a sub-chronic study in a laboratory animal. Following the U.S. EPA (1993) guidance provided above, any MOE less than 300, as determined by the TSG approach, may be of concern and warrants case-by-case evaluation to consider all relevant information in making a risk management decision regarding PBDEs.

In looking at the range of MOEs presented in Table 21, which are based on different human tissue concentrations, it appears there is significant concern for highly exposed individuals to BDE-47, BDE-99, and BDE-153. This is based on the finding of MOEs less than ten using the highest measured human tissue concentration for these congeners. BDE-99 presents the greatest concern, as the MOE is less than one under this scenario. This indicates that people who may be highly exposed to PBDEs have levels of this congener in their body that are greater than the levels in animals that produced adverse effects. In addition, the finding of MOEs of 50 and 200, based on the highest median tissue concentration for BDE-99 and BDE-47, respectively, suggests concern also exists for much larger percentages of the population that may be exposed to lower levels of PBDEs.

REGULATORY ACTIONS AND LEGISLATION

With levels of PBDEs in the environment increasing, legislative bans have recently been passed and more are being considered. Following is a summary of regulatory and legislative activity for Michigan, other states, the U.S. EPA, and elsewhere.

Michigan

CMR

The current CMR is listed in the Wastewater Reporting Rules (R299.9001 – R299.9007 of Part 31, Water Resources Protection, of the Natural Resources and Environmental Protection Act, 1994 PA 451, as amended) and consists of the following: metals that are highly toxic to aquatic life; substances frequently found in groundwater; and substances considered persistent, bioaccumulative, and toxic. In 2002, environmental stakeholders requested that the MDEQ add PBDEs to the CMR. Based on a review of the available scientific literature, staff concluded that there is sufficient justification to place all of the PBDE congeners on the CMR (MI/DEQ/WB-8/03). The TSG supports this recommendation.

Legislation

House Bill 4406 became PA 562 of 2004, effective on January 3, 2005. This bill states that beginning on June 2, 2006, a person shall not manufacture, process, or distribute a product or material containing more than one-tenth of 1% of Penta-BDE. House Bill 4406 does not apply to original equipment manufacturer replacement parts or the processing of recyclables containing Penta-BDE in compliance with applicable laws. Senate Bill 1458 also became PA 526 of 2004, effective on January 3, 2005. This bill has similar language, but deals exclusively with Octa-BDE (Michigan Legislature 2004a, 2004b).

On January 24, 2006, House Bill 5573 was introduced. It bans the manufacture, processing, or distribution of a product or material containing Deca-BDE beginning on June 1, 2007, but provides exemptions for original equipment manufacturer replacement parts and recyclables containing Deca-BDE. The legislation allows that the MDEQ may establish a PBDE advisory committee to assist them in determining the risks posed by PBDEs (other than Penta- and Octa-BDE) and their alternatives.

Legislation in Other States

California

In August 2003, California was the first state to limit the use of certain PBDEs. Assembly Bill 302, states the following, “On and after January 1, 2008, a person may not manufacture, process, or distribute in commerce a product or a flame-retarded part of a product, containing

more than one-tenth of 1% of Penta-BDE or Octa-BDE, by mass." The phase out date was revised to January 1, 2006, in September 2004 (California State Assembly, 2003).

In February 2006, the California Environmental Protection Agency (Cal/EPA) published a report entitled, "Polybrominated Diphenyl Ethers: Recommendations to Reduce Exposure in California" (Cal/EPA, 2006). This report was in response to a directive by the Cal/EPA Secretary for the formation of a workgroup of representatives from the Cal/EPA Boards, Departments and Office, and the California Department of Health Services. The workgroup's task was to consider the nature and extent of the PBDE problem and to recommend actions the Cal/EPA could undertake to mitigate exposures and reduce risks of potential PBDE health effects. The principal focus of the report is to address continuing exposures of Californians to PBDEs after June 1, 2006, which is the date of the prohibition established by the legislation. The report concludes that direct exposure to Deca-BDE appears to pose a lower human health risk than those of the other PBDEs, due to lower toxicity, absorption, and generally lower environmental concentrations. However, Deca-BDE is the predominant PBDE measured in indoor dust, and its risks require further evaluation. Use of Deca-BDE may result in exposure to the more toxic lower brominated PBDEs, based on studies indicating that Deca-BDE breaks down by the actions of sunlight, heat, and bacteria to the lower brominated forms.

Recommendations for near-term actions, such as outreach and education and voluntary pollution prevention are intended to reduce PBDE exposures. Longer-term recommendations for further environmental monitoring would increase the scientific database for decision making and consideration of specific regulatory actions. The Cal/EPA recommends developing health guidance levels for the purpose of establishing acceptable environmental levels and assessing the need for further regulations.

Hawaii

Hawaii passed a bill in June 2004, which prohibits the manufacture, processing, or distribution of a product or flame retarded part of a product containing more than 0.1% by mass of Penta-BDE or Octa-BDE, or any other chemical formulation that is part of these classifications, on or after January 1, 2006 (Hawaii State Legislature, 2004).

New York

New York enacted a bill in August 2004, which prohibits the manufacture, process, or distribution of Penta- and Octa-BDE by January 1, 2006. A task force on flame retardant safety was also established by the bill. The purpose of the task force is to study the risks of and alternatives to Deca-BDE (New York State Assembly, 2004).

Maine

In April 2004, Maine passed legislation which reduces contamination from PBDEs. The title of the legislation is, "An Act to Reduce Contamination of Breast Milk and the Environment from the Release of Brominated Chemicals in Consumer Products." The first section of the bill prohibits the sale of products containing more than 1% Penta-BDE or Octa-BDE beginning January 1, 2006. Section 2, indicates that the legislature intends to reduce risks associated with Deca-BDE, either through the implementation of risk management measures or by prohibition of the sale of products that contain more than 1% Deca-BDE, beginning January 1, 2008, assuming a safe alternative will be available. The Department of Environmental Protection is required to review emerging information on PBDEs and other BFRs and report annually to the Legislature's

Committee on Natural Resources beginning January 5, 2005 (Maine State Legislature). As a result of the findings of the first annual report, the legislature is recommended to keep in place the 2008 ban on Deca-BDE, while the departments continue to review the ongoing and planned studies of this chemical's toxicity, environmental fate and transport, and alternatives. The findings upon which this recommendation are made include: Deca-BDE bioaccumulates and concentrates up the food chain; Deca-BDE is neurotoxic in developing rodents; total PBDE levels in humans are not yet at levels shown to be harmful to rodents. However, Deca-BDE's contribution to total PBDE body burdens is unclear, due to incomplete data on the breakdown of Deca-BDE. Deca-BDE is broken down by sunlight and living organisms, but the full identify and fate of the breakdown products in the environment are not well studied, suggesting that Deca-BDE's contribution to total PBDE levels may be underestimated.

Washington

The Washington State Departments of Ecology and Health jointly wrote an interim chemical action plan for PBDEs (Washington State, 2004). This report is the result of a directive dated January 2004, from the Governor of Washington, to develop a plan to reduce the threat of PBDEs in the environment. The final chemical action plan was released January 19, 2006 (Washington State, 2006). Following are some of the key recommendations presented in the report: 1) prohibit the manufacture, distribution, or sale of new products containing Penta-BDE and Octa-BDE in Washington. The ban may include an exemption for new products containing recycled material from products that contained Penta-BDE and Octa-BDE, pending further review; 2) ban Deca-BDE provided safer, effective, affordable alternatives are found or upon additional evidence of Deca-BDE harm; 3) if safer alternatives are not available, work with stakeholders to explore incentives for their manufacture; 4) establish appropriate disposal and recycling practices for products containing PBDE flame retardants; 5) work with other states and interested parties to improve the chemical policy of the U.S.; 6) restrict the state's purchase of products containing PBDEs; and 7) develop methods and materials for educating the public on how to minimize PBDE exposures.

Oregon

Senate Bill 962 was enacted on July 14, 2005. The statute prohibits the introduction or delivery for introduction into commerce of any product containing more than 1/10 of 1% by mass of Penta-BDE or Octa-BDE, on or after January 1, 2006. Two exemptions are provided. The statute also requires that the state track all brominated flame retardants and report to the legislature.

Maryland

In May 2005, the Maryland Legislature passed a bill which prohibits the sale, manufacture, processing, or distribution of products containing more than 1/10 of 1% of Penta- or Octa-BDE by October 1, 2008. The Department of Environment is required by the legislation to report on uses of Deca-BDE and to evaluate potential restrictions on its sale and use by January 8, 2007.

Massachusetts

Two bills have been proposed in Massachusetts (H 2275 and S 1268), which address alternatives to the use of toxic chemicals. Penta-BDE is on the list of chemicals to be phased out. The bills were heard in September 2003, in the Joint Committee on Natural Resources and

Agriculture and were eligible for the Executive Session. Massachusetts is also considering legislation to reduce the use of PBDEs, along with nine other commonly used toxic chemicals in the state.

Illinois

Effective January 1, 2006, the Brominated Flame Retardant Prevention Act provides that a person may not manufacture, process, or distribute in commerce a product, or a flame retarded part of a product containing more than 1/10 of 12% of Penta-BDE or Octa-BDE by mass. Three exemptions are identified. In January 2006, a report entitled, "Deca-BDE Study: A Review of Available Scientific Research" was submitted to the Illinois General Assembly and the Governor (Illinois EPA, 2006). This report was written in response to Public Act 94-100, which required the Illinois Environmental Protection Agency to review the latest available scientific research on Deca-BDE. The Act posed questions related to the following five issues: bioaccumulation in humans and the environment; health effects resulting from human exposure; health effects resulting from degradation products; and available effective alternatives. Following is a summary of the findings related to the issues:

1) It was determined that Deca-BDE is bioaccumulating in the environment and that levels are increasing in the following media: sediments, some top predators, and possibly human blood and breast milk.

2) Humans are exposed to Deca-BDE through a variety of sources such as diet, the workplace, and the home. The primary source for adults is diet. While for infants and small children, the primary sources are breast milk and house dust.

3) The report identified the following health effects as the most important from exposure to Deca-BDE: liver, thyroid, reproductive/developmental, and neurological effects. However, significant data gaps in the Deca-BDE toxicity database have been identified. Two recent studies indicate that exposures in the range of doses causing adverse effects in laboratory animals could be occurring.

4) Deca-BDE can be broken down into more harmful chemicals by ultraviolet light, direct sunlight, and also by metabolic processes in animals and microorganisms. Uncertainty and controversy exists about the extent of breakdown by light under environmentally relevant conditions. Uncertainty also exists related to the health implications of these breakdown products. The report concludes that the current information regarding Deca-BDE's breakdown products is insufficient to confidently address the issue.

5) Effective, although more costly alternatives exist for most of the plastic, textile and fabric uses of Deca-BDE. These alternatives will likely reduce risks while maintaining an adequate level of flame retardant performance. However, more research is needed to better evaluate the health and environmental impacts of these alternatives, since significant toxicity data gaps exist for many of them.

Legislation related to PBDEs (some are specifically for Deca-BDE) has also been introduced in Hawaii, Illinois, Massachusetts, Minnesota, Rhode Island, Washington, Montana, and Connecticut.

The Federal Government

High Production Volume

The U.S. EPA has included PBDEs in the High Production Volume (HPV) evaluation and testing programs. The HPV program is designed to ensure the American public has access to basic health and environmental effects data for those chemicals that are produced in the highest volumes in the U.S. The HPV Challenge Program encourages chemical manufacturers to voluntarily test those chemicals for which little or no health or environmental effects data are publicly available.

Voluntary Children's Chemical Evaluation Program

Penta-, Octa-, and Deca-BDE are three of the 23 chemicals identified in the pilot program for the U.S. EPA's VCCEP. The VCCEP is intended to provide data which will enable the public to understand the potential health risks to children from exposure to certain chemicals. The U.S. EPA asked companies that manufacture and/or import 23 chemicals that have been found in human tissues and in the environment in various monitoring programs, to volunteer to sponsor their evaluation in Tier 1 of a pilot of the VCCEP. Thirty-five companies and ten consortia responded and volunteered to sponsor 20 chemicals. A report from the American Chemistry Council's Brominated Flame Retardant Industry Panel (BFRIP) was submitted for Penta- and Octa-BDEs and another for Deca-BDE. The information submitted by the sponsor is evaluated in a peer consultation by a group of scientific experts with extensive and broad experience in toxicity testing and exposure evaluations. Toxicology Excellence for Risk Assessment (TERA) was hired to organize and facilitate the peer consultations and forward the results to the U.S. EPA and the sponsors concerning the adequacy of the assessments and the need for development of any additional information to fully assess risks to children. The U.S. EPA will consider the results of the peer consultation and announce whether additional higher tier information is needed. If additional information is needed, sponsors will be asked to volunteer to provide the next tier of information. If additional information is not needed, the U.S. EPA and the sponsors will cooperate to conduct appropriate risk communication, and if necessary, risk management.

The peer consultation meetings for Penta- and Octa-BDEs and for Deca-BDEs were held in 2003. The peer consultation panel for Deca-BDE completed their report on September 30, 2003. The report is available at TERA's web site. The U.S. EPA's Data Needs Decision Document of Deca-BDE was published in June of 2005. A letter was sent on August 25, 2005, to the BFRIP manager indicating that the assessments prepared by BFRIP for Tier 1 of VCCEP are not sufficient to adequately characterize its risks to children. The conclusion is that the assessment activities for Deca-BDE need to proceed to Tier 2 of VCCEP to more fully address the chemical's fate and transport in the environment. The BFRIP manager responded with a commitment for a Tier 2 submission for the VCCEP pilot program. The Panel's intent was to begin developing information for its Tier 2 submission in 2006.

The peer consultation reports for Penta- and Octa-BDEs were completed January 22, 2004. The U.S. EPA's Data Needs Decision Documents for Penta- and Octa-BDE were both completed June, 2005. A letter was sent to the Great Lakes Chemical Corporation on August 25, 2005. The U.S. EPA determined that additional data beyond the Tier 1 assessments are needed to characterize the risks to children. The U.S. EPA specifically cited the need for two generation reproductive toxicity studies for both chemicals. The Great Lakes Chemical Corporation responded January 6, 2006, indicating they decided not to sponsor either of the two substances under the remaining two tiers of the VCCEP program. The basis for their decline to

sponsor further study is the company's 2003 decision to cease the manufacture of both Penta- and Octa-BDE.

Toxic Release Inventory

Deca-BDE is the only PBDE product required to have releases reported under the Superfund Amendments and Reauthorization Act, Title III, Section 313. As a result, data are available for this compound in the Toxic Release Inventory (TRI). In 2005, Michigan's TRI reports that 5,122 pounds of Deca-BDE were released into the air from stack or point air emissions. No releases to surface water or on-site surface impoundments were reported. A total of 23,999 pounds were released both on and off-site and includes disposal transfers. The total number of pounds released, both on and off-site for 1996 through 2004, are 38,932, 36,490, 41,573, 55,704, 45,163, 53,844, 25,588, 25,002, and 30,892 pounds per year, respectively. The TRI is not an exhaustive list of releases, since only those facilities meeting specific criteria are required to report. Under the TRI, an average of 1,000 facilities report annually.

Significant New Use Rule

Under section 5(a)(2), of the Toxic Substances Control Act, the U.S. EPA issued a draft Significant New Use Rule (SNUR) for Penta- and Octa-BDE on December 6, 2004. Manufacturers and importers are required to notify the U.S. EPA at least 90 days before commencing the manufacture or import of Penta- and Octa-BDE on or after January 1, 2005. This notification requirement provides the U.S. EPA with an opportunity to evaluate any intended new use and associated activities and, if necessary, a prohibition of that activity before it occurs. February 4, 2005, marked the end of the comment period.

PBDE Project Plan

In March of 2006, the U.S. EPA released the Polybrominated Diphenyl Ethers (PBDEs) Project Plan (Plan) (U.S. EPA, 2006). The Plan is posted on the U.S. EPA's website at www.epa.gov/oppt/pbde. The website will be updated periodically to report on the progress on the various activities. The Plan includes a brief summary of relevant information on PBDEs, along with an outline of the agency's activities related to PBDEs and similar chemicals. Some of the activities include:

- A SNUR proposed by the U.S. EPA
- An evaluation of alternatives to PBDEs in furniture applications
- An analytical measurement of PBDEs in 340 fish samples collected from 166 lakes and reservoirs
- A review of the available toxicology data and the development of toxicological profiles for Tetra-, Penta-, Hexa-, and Deca-BDE under the Integrated Risk Information System (IRIS) program
- The Centers for Disease Control and Prevention (CDC) is conducting a national survey of PBDE body burdens in the population of the U.S.

- The NTP is conducting a sub-chronic toxicity study of Penta-BDE in lab animals. Also being conducted are pharmacokinetic studies of three PBDE congeners.

- The U.S. Department of Agriculture is studying the absorption and metabolism of PBDEs in animals and has measured them in meat and poultry.

- The U.S. Geological Survey is studying the migration of PBDEs from plastics in computers and their presence in the indoor environment.

The Plan also identifies the four areas where the U.S. EPA is focusing its activities. These four areas or objectives are:

1. Assess substitutes for Penta- and Octa-BDE;

2. Assess and evaluate Deca-BDE;

3. Assess risks of Penta- and Octa-BDE; and

4. Track developments concerning other brominated flame retardants of interest.

Specific to Objective 2, the U.S. EPA is currently conducting a review of the toxicology data for Deca-BDE. An update to the IRIS file for Deca-PBDE should be completed this year. In its monitoring of ongoing and planned research on the toxicity of Deca-BDE and its metabolites, the U.S. EPA is focusing on a developmental neurotoxicity study sponsored by the EU and studies conducted by the Flame Retardants Integrated Risk Assessment for Endocrine Effects (FIRE) in Europe. The FIRE is presently conducting a 28-day toxicity study in rats; additional animal studies may follow. Through the VCCEP program, the U.S. EPA determined that further information is necessary to address Deca-BDE's potential to degrade to other substances in the environment. As a result, the U.S. EPA will investigate the environmental fate and metabolism of Deca-BDE. Of particular interest is the potential for Deca-BDE to form lower brominated congeners by debromination in the environment. This year, the U.S. EPA is also planning to write a review paper on all the available information related to the environmental fate of Deca-BDE. This paper will specifically assess the potential for natural environmental mechanisms to debrominate Deca-BDE. Further, the paper will assess the rate, extent, and conditions under which debromination may occur, and whether debromination of Deca-BDE is likely to be a significant source of lower brominated PBDEs in humans and wildlife. More broadly, the U.S. EPA will conduct an interim review of all available scientific information related to Deca-BDE in 2006 and 2007. This review will include the environmental fate paper just mentioned, the CDC data on Deca-BDE body burdens in the U.S., data from the U.S. EPA's National Lake Fish Tissue Study, information developed under VCCEP, and whatever other studies that may become available on Deca-BDE. Upon completion of this review, the U.S. EPA will determine whether additional research, risk assessment, or regulation is warranted.

The Plan includes three appendices. Appendix A presents a summary of the current scientific understanding of PBDEs. Appendix B presents selected international activities. Appendix C presents a listing of PBDE research and assessment activities conducted by or funded by the U.S. EPA. On December 22, 2006, the U.S. EPA released Draft Toxicological Reviews including RfDs for BDE-47, BDE-99, BDE-153, and Deca-BDE for public comment and peer review.

International Overview

European Union

In early 2003, the EU adopted a directive that bans the marketing and use of Penta- and Octa-BDE in all consumer products beginning on August 15, 2004. In addition, a separate European-wide ban under the Restriction on Hazardous Substances (RoHS), which has a specific focus on electronics, will eliminate all PBDEs in electronics by 2006. This ban allows for an exemption for Deca-BDE, if supported by a risk assessment. The Human Health Draft of the Draft Update Risk Assessment of Deca-BDE was completed by France in February 2004, (European Commission Joint Research Center, 2004a). This update concluded that there is presently no need for further information and/or testing or risk reduction measures beyond those which are currently being applied. This conclusion was related to the neurotoxicity of Deca-BDE. The Final Environmental Draft of the Draft Update Risk Assessment was completed by the United Kingdom in May 2004 (European Commission Joint Research Center, 2004b). This update resulted in two conclusions about Deca-BDE. The first conclusion was a need for further information and/or testing regarding the determination that Deca-BDE is persistent, bioaccumulative, and toxic. The assessment also indicated that testing and additional information is needed to monitor the potential for Deca-BDE to degrade to more toxic and bioaccumulative chemicals but, nonetheless, concluded that further risk reduction are not presently needed for Deca-BDE.

The Scientific Committee on Health and Environmental Risks (SCHER), which is a committee of physicians and professors acting in an advisory role to the EU, commented in March 2005, that they disagree with the United Kingdom's recommendation that risk reduction measures are unnecessary. In response, the EU Joint Research Center released an update to the Environmental Risk Assessment disagreeing with the SCHER, but incorporating the SCHER's recommendations for a regular review of any new information relating to Deca-BDE. The report also discusses the need for further study of the debromination of Deca-BDE. A final decision regarding the exemption of Deca-BDE from the RoHS ban will be made by the Court of Justice.

Summary information on PBDE related activities in other countries can be obtained from the Washington State PBDE CAP.

UNITED STATES MANUFACTURING OF PENTA- AND OCTA-BDES

The main U.S. manufacturer of Penta-BDE and Octa-BDE ceased production of these two widely used PBDE formulations by the end of 2004, as part of a voluntary agreement with the U.S. EPA. A statement released jointly by the U.S. EPA and by the Great Lakes Chemical Corporation of West Lafayette, Indiana states that the agreement was "based on potential concerns associated with the continued use of the chemicals."

SAFE ALTERNATIVES

The goal of removing PBDEs from commerce and reducing environmental levels needs to be accompanied with the use of alternatives proven to be safe for adequate fire protection and to assure the alternatives will not present unacceptable risks to public health or the environment. It is critical that the replacement chemicals be properly evaluated to ensure they will not become environmental contaminants of the future.

CONCLUSIONS AND RECOMMENDATIONS

The conclusions and recommendations from the 2004 Draft Report is presented in Appendix B of this report. The following conclusions and recommendations are based upon the updated information presented in this paper.

Important accomplishments have been made with respect to PBDEs since the 2004 draft. For instance, legislation banning the manufacture, use, and distribution of Octa- and Penta-BDE in Michigan was passed in 2004; the only manufacturer of these two PBDE congeners agreed to end production by the end of 2004; and additional data on levels of PBDEs in Michigan's environment were collected. However, since Deca-BDE was not addressed in the PBDE legislation, it was considered prudent to assess whether restrictions should be placed on its use. Although Deca-BDE is less toxic than the lower brominated PBDEs, it has been shown to cause neurodevelopmental effects and reductions in thyroid hormone levels in developing animals. There is a significant potential for exposure to Deca-BDE, since it has been found in household dust at levels higher than the other PBDE congeners. Although previously thought to be biologically unavailable, Deca-BDE has been detected in the tissues of humans, fish, birds, polar bears, and sharks. Deca-BDE has been detected in the Great Lakes region. For instance, Deca-BDE has been measured in fish and sediments in Lake St. Clair, in the Shiawassee River, and in the Saginaw River and Bay. Deca-BDE has been shown to degrade in the environment, however, the extent and significance of this process is unclear. It is also unclear whether Deca-BDE is a significant source of the lower, more toxic PBDEs.

It was determined that information is insufficient to conduct a quantitative risk assessment with an acceptable level of uncertainty for Deca-BDE. While there are many uncertainties associated with quantifying risk from environmental exposure to Deca-BDE, the available data suggest reason for concern and support action to limit uses and move to safer alternatives. Considering currently available information, the following recommendations are made.

1) Support legislation banning Deca-BDE. This recommendation is contingent on the availability of a safe alternative and is made for the following reasons:

    - While there are no trend data for Deca-BDE specifically, the trend data for the other PBDE congeners in human tissues are increasing. If similar increasing trends occur for Deca-BDE, this would result in higher body burdens in the future that could ultimately represent an unacceptable level of risk.

    - The data for levels of Deca-BDE in human tissues are very limited, and as a result, the full range of concentrations in humans is unknown. Highly exposed humans may have greater amounts of Deca-BDE in their bodies, making the associated risks higher, as well.

- While the existing database for levels of Deca-BDE in children is extremely limited (based on two children from a family in California); the concentrations of Deca-BDE in the tissues of the children were higher than in the adults. Household dust has been shown to contain high concentrations of PBDEs and typically, Deca-BDE is the most abundant congener. Household dust may be a significant exposure pathway. This is a concern since children ingest a greater amount of house dust than adults due to their frequent hand-to-mouth activity.

- The primary source of exposure to Deca-BDE is likely to come from its use in household consumer products. A ban on the use of Deca-BDE in household products would significantly reduce exposures and subsequently reduce body burden levels in humans.

- The effects of exposure to multiple PBDE congeners potentially are additive. If the effects are additive, the risks could be significantly greater than those related only to Deca-BDE.

- As discussed earlier in the document, evidence is available which demonstrates that Deca-BDE debrominates to the more toxic PBDE congeners. It is not known to what extent this occurs in the environment, however this possible contribution adds to the weight of evidence supporting legislation banning Deca-BDE.

- Although Deca-BDE is absorbed to a lesser degree and metabolized and excreted to a greater degree than the lower brominated congeners, it produces some metabolic by-products that may be biologically active. There are many unknowns and uncertainties surrounding the toxicokinetics of Deca-BDE however, the information available presents reason for concern.

2) Insure that Penta- and Octa-BDE bans are effective and being followed. If appropriate, request the MDEQ Environmental Science and Services Division prepare educational materials for the public. Pursue development of an environmental monitoring program as a gauge to evaluate the success of the bans and to monitor the presence and trends of Deca-BDE.

3) Investigate whether safer alternatives for PBDEs are available. Evaluate any replacement chemicals for safety and environmental persistence to determine the need for monitoring their presence in the environment.

4) Monitor and evaluate all the U.S. EPA, the FIRE, and the EU Deca-BDE studies and reports, along with peer reviewed scientific studies. When adequate data are available, develop standards and criteria.

5) Since PBDEs are present in house dust, with concentrations of Deca-BDE being the highest, pursue educational materials or guidelines for reducing exposures to PBDEs, particularly for children.

6) The Toxic Substances Control Act (TSCA), signed into law in 1976 and implemented in 1979, requires that Premanufacture Notices be submitted for all new chemicals prior to their introduction into commerce. This does not apply to chemicals already in commerce prior to TSCA's implementation unless the U.S. EPA promulgates a rule under

Section 4. PBDEs were already used in commerce prior to 1979. Since the list of chemicals in commerce prior to 1979 totals more than 60,000 chemicals, the U.S. EPA has not pursued the Section 4 rule promulgation option. This has resulted in the U.S. EPA's reliance on voluntary data submission; however, very few chemicals have been addressed in this manner. This explains why chemicals with very little information are permitted for use in the U.S. The TSG recommends that the MDEQ pursue options for contributing to changes in the chemical policy in the U.S.

7) Consider implementing some of the monitoring recommendations provided in the 2004 PBDE Draft Report.

ACRONYMS

ABS ..... Acrylonitrile-butadiene-styrene
Ah ..... Aryl hydrocarbon
ATSDR ..... Agency for Toxic Substances and Disease Registry
AWR ..... Annual Wastewater Reporting
BFR ..... Brominated Fire Retardants
BFRIP ..... Brominated Flame Retardant Industry Panel
bw ..... Body Weight
^{14}C ..... Carbon^{14}
CAS ..... Chemical Abstract Service
CAP ..... Chemical Action Plan
CDC ..... Centers for Disease Control and Prevention
CH ..... Congenital Hypothyroidism
CMR ..... Critical Materials Register
CYP1A ..... Cytochrome P4501A
DDT ..... Dichlorodiphenyltrichloroethane
dw ..... dry weight
EPA ..... United State Environmental Protection Agency
EROD ..... Ethoxyresorufin-o-deethylase
EU ..... European Union
EWG ..... Environmental Working Group
FIRE ..... Flame retardants Integrated Risk assessment for Endocrine
g/kg ..... Grams per Kilogram
g/mL ..... Grams per Millimeter
GD ..... Gestation Day
GI ..... Gastrointestinal
Hg ..... Hemoglobin
HPV ..... High Production Volume
HQ ..... Hazard Quotient
IRIS ..... Integrated Risk Information System
IUPAC ..... International Union of Pure and Applied Chemistry
kg/yr ..... Kilograms per Year
Km ..... Kilometer
LC_{50} ..... Lethal Concentration to 50% of the Population
LD_{50} ..... Lethal Dose to 50% of the Population

LOAEL ..... Lowest Observed Adverse Effect Level
LOEL ..... Lowest Observed Effect Level
Log K_{OC} ..... Log Organic-Carbon Partition Coefficient
Log K_{OW} ..... Log Octanol-Water Partition Coefficient
m3 ..... Cubic Meter
MDEQ ..... Michigan Department of Environmental Quality
MDL ..... Method Detection Limit
MeO ..... Methoxylated
mg/kg ..... Milligrams per Kilogram
mg/kg/day ..... Milligrams per Kilogram per day
mg/L ..... Milligrams per Liter
mg/m^3 ..... Milligrams per Cubic Meter
mm ..... Millimeter
MOE ..... Margin of Exposure
MSW ..... Municipal Solid Waste
NAS ..... National Academy of Science
n.d. ..... Not Detected
ng/g ..... Nanograms per Gram
ng/L ..... Nanograms per Liter
ng/m^2 ..... Nanograms per Square Meter
NOAEL ..... No Observed Adverse Effect Level
NOEL ..... No Observed Effect Level
NTP ..... National Toxicology Program
OH ..... Hydroxy
PBB ..... Polybrominated biphenyls
PBDE ..... Polybrominated diphenyl ether
PCB ..... Polychlorinated biphenyls
PBT ..... Persistent Bioaccumulative and Toxic
$pg/cm^2/yr$ ..... Picograms per Square Centimeters per Year
pg/g ..... Picograms per Gram
pg/L ..... Picograms per Liter
pg/m^3 ..... Picograms per Cubic Meter
PND ..... Post Natal Day
POP ..... Persistent Organic Pollutants
PPM ..... Parts per Million
PPB ..... Parts per Billion
R^2 ..... Regression Coefficient
RfD ..... Reference Dose
RL ..... Reporting Limit
RoHS ..... Restriction on Hazardous Substances
RSC ..... Regional Science Council
SCHER ..... Scientific Committee on Health and Environmental Risks
SNUR ..... Significant New Use Rule

$T_{1/2}$ ..... Half-life
T_3 ..... Triiodothyronine
T_4 ..... Thyroxin
TCDD 2,3,7,8-Tetrachlorodibenzo-*p*-Dioxin
TERA ..... Toxicology Excellence for Risk Assessment
TRI ..... Toxic Release Inventory
TSCA ..... Toxic Substance Control Act
TSG ..... Toxics Steering Group
TSH ..... Thyroid Stimulating Hormone
μg/g ..... Micrograms per Gram
μg/kg ..... Micrograms per Kilograms
μg/L ..... Micrograms per Liter
UDPGT ..... Urinediphosphate-glucuronosyltransferase
UF ..... Uncertainty Factor
VCCEP ..... Voluntary Children's Chemical Evaluation Program
WB ..... Water Bureau
WHO ..... World Health Organization
wwt ..... Wet Weight

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APPENDIX A

COMMENTS ON THE 2004 MICHIGAN PBDE BACKGROUND PAPER

The PBDE Background paper was sent to Dr. Gilberto Alvarez, Chair of the U.S. EPA Region 5 Regional Science Council (RSC) and to the U.S. EPA Representative to Region 5 RSC's State Tribal Science Network, for distribution. The report was also forwarded to environmental group representatives who were instrumental in initiating the proposed legislation. The PBDE paper received further distribution from these initial contacts. The paper was also placed on the MDEQ website where it was accessed by additional reviewers.

Comments were received from thirteen reviewers, although most reviewers only made general positive comments about the report's thoroughness and expressed an interest in the final report. Several reviewers also provided citations for documents or copies of scientific articles pertinent to the issue. Following are summaries of the substantive comments submitted to the MDEQ.

Reviewer 1: Ms. Tracey Easthope
Ecology Center

Comments:

- Include information from the February 2004, Body of Evidence. According to Ms. Easthope, information in this report provides sufficient evidence that Deca-BDE should be banned along with Penta- and Octa-BDE.

- Include information about biomagnification of Deca-BDE in birds and problems with analytical methods, which may be partially why Deca-BDE is often not detected in samples.

- Include information on safe alternatives to PBDEs.

Response:

Much of the information provided in the Body of Evidence document was also reported in this paper. The information in the second bullet is in the report. Although alternative products are important, the scope of this document does not allow for inclusion of this information.

Reviewer 2: Dr. Linda S. Birnbaum
U.S. EPA National Health and Environmental Effects Research Laboratory

Comments:

- PBDEs should not be treated as a homogenous group, since the three commercial mixtures have different properties, uses, and toxicities.
- Make sure all studies discussed in the report have appropriate references.
- It is possible to estimate body burden in animals from the existing literature, which can then be used to compare to the body burdens in humans. The body burden in humans can be estimated from the lipid adjusted values from serum or breast milk, with certain assumptions.
- Dr. Birnbaum provided a list of five articles for incorporation into the report.
- Include in the discussion on thyroid toxicity that the induction of UDPGTs in the liver, leading to rapid conjugation and elimination of the T_4-glucuronide, may be a major mechanism occurring in the thyroid.

Response:

The report acknowledges the different properties, uses, and toxicities of the different commercial mixtures. We attempted to incorporate references for cited information. The information in Dr. Birnbaum's last bullet was incorporated.

Reviewer 3: Dr. Wayne Whipple
U.S. EPA Region 5, Central Regional Laboratory

Comments:

- Somewhat confusing statements about the degradation of Deca-BDE on page 13.
- Mono-BDE should be included in the list of PBDE congeners.
- The potential for breakdown of Deca-BDE to lower brominated congeners may suggest including Deca-BDEs with a ban of Penta- and Octa-BDEs.
- Electronic waste should be included in the list of potential sources in the Environmental Media section.

Response:

This information was considered and incorporated, as appropriate.

APPENDIX B

2004 DRAFT REPORT
POTENTIAL RISKS, CONCLUSIONS, RECOMMENDATIONS

Potential Risks

The ideal manner in which to evaluate potential risks to humans is to compare body burden levels in humans to body burden levels in experimental animals at which adverse effects were seen. However, body burden animal data is currently unavailable. Comparing intake levels, although less ideal, is another way comparisons can be made between humans and experimental animals to quantify potential risks to humans. All exposures to humans, including consumption of contaminated fish, would need to be combined to estimate daily intake levels for humans. Exposure data are currently very limited. The existing fish data are limited such that estimates of intake would be highly uncertain. Most of the existing Great Lakes fish data for PBDEs are for whole fish tissue. The only fillet data currently available are the Coho and Chinook salmon data recently released by the U.S. EPA. As a result, an evaluation of potential risks can only be conducted in a qualitative manner at this time.

Adverse effects are seen in experimental animals at dose levels ranging from 0.6-30 mg/kg/day. Humans are clearly being exposed to PBDEs from a variety of sources, as evidenced by increasing PBDE levels in the environment and in human blood, breast milk, and breast adipose tissue. Levels of PBDEs in North America appear to be doubling every two to five years. PBDEs are present in Great Lakes fish. Food products in Michigan, although not yet studied, are assumed to contain PBDEs as shown via results from food products collected elsewhere in the country. Indoor dust samples collected in Massachusetts contained significant levels of PBDEs. We expect that concentrations of PBDEs in indoor dust samples in Michigan would be similar. Levels in the environment are increasing to alarming levels and at an alarming rate. The combination of the toxicity data in laboratory animals and the rapidly increasing levels in the environment, wildlife, and humans warrants concern about these environmental contaminants.

The scientific evidence for Deca-BDEs is more limited and less convincing, since Deca-BDE does not appear to be as bioavailable as the lower brominated PBDEs. However, recent data suggests that Deca-BDEs cause neurodevelopmental effects in rodents, may be debrominated in carp, and are present in humans.

Conclusions and Recommendations

The information presented in this document indicates there are insufficient toxicity and exposure data to conduct a thorough quantitative risk assessment for PBDEs. However, the exponential increase of PBDEs in biota (herring gull eggs and lake trout), the bioaccumulative and persistent nature of PBDEs, the rapidly increasing levels in human blood and breast milk, and their toxicity to laboratory animals, provide sufficient evidence to support a ban on the commercial use of Penta- and Octa-PBDEs in Michigan. The scientific evidence for Deca-BDEs is more limited and less convincing, since Deca-BDE does not appear to be as bioavailable as the lower brominated PBDEs. However, recent data suggests Deca-BDEs cause neurodevelopmental effects in rodents, may be debrominated in carp, and are present in humans. As such, it may be appropriate to include them in future legislation. The TSG will continue to monitor the published scientific literature for the purpose of locating additional information to support proposed legislation banning Deca-BDEs along with Penta- and Octa-BDEs.

The TSG supports modification to House Bill 4406. It is recommended that Penta- and Octa-BDEs be specified in the ban. Deca-BDEs should be considered through a risk management decision making process, which considers all pertinent and recently published scientific data. The goal of modifying the bill would be to minimize and ultimately eliminate the release of Penta- and Octa-BDEs into the environment through a ban on their manufacture, processing, and distribution in Michigan. Following are some suggestions for modification to the proposed legislation:

- Penta- and Octa-BDEs should be specified in the legislation;
- The most effective way to prevent the continuation of rapidly increasing levels of PBDEs into the environment is through legislation, which prevents the manufacturing, processing, and distribution of goods containing these commercial PBDE products;
- The burden of a MDEQ demonstration that PBDEs do not pose an unacceptable risk should be removed. If such a demonstration must be made to prevent a ban, industry should make the demonstration, and
- Reporting of releases to surface water would not be necessary, since this would be done through the Annual Wastewater Reporting Program, once PBDEs are added to the CMR. A requirement to annually report other releases of PBDEs could be maintained in the proposed legislation.

MDEQ Programs

The MDEQ does not currently address PBDEs in any of its regulatory programs. The environmental media in which PBDEs are present and the sources from which they originate must be identified. Releases likely to contain PBDEs should be the initial focus, such as waste types identified in the literature as containing PBDEs, or processes known to use PBDEs. Once additional information is available on specific sources and releases identified through monitoring programs, the MDEQ can then consider approaches for minimizing PBDE releases into the environment. Specific suggestions for evaluating potential impacts of PBDEs associated with existing MDEQ programs include:

- Review the recently released data on PBDE levels in fish in the Great Lakes region and determine whether additional fish need to be analyzed for the fish contaminant monitoring program;
- Include PBDEs for analyses of sediment samples including those associated with dredging, areas of concern investigations, and surveys;

- Monitor PBDEs in biosolids used in land application;

- Consider including PBDEs in sampling or monitoring plans associated with the National Pollutant Discharge Elimination System discharge program;

- Identify the types of Part 201 facilities where PBDEs are likely to be present (perhaps through a preliminary monitoring program), and require that PBDEs be included in the list of analytical parameters for those types of sites identified;

- Consider inclusion of PBDEs when establishing monitoring requirements for air permits for sources that may emit PBDEs, e.g., municipal solid waste and sewage sludge incinerators or sources that use PBDEs in their manufacturing process;

- Include PBDEs for analyses of samples the MDEQ collects from municipal solid waste landfills (leachate and/or groundwater), and consider adding PBDEs to monitoring programs if PBDEs are detected;

- Include PBDEs for analysis of statewide soil survey samples, and

- Consider including analyses for PBDEs to any other sampling events or monitoring programs where PBDEs may be present.

Consideration should be given to the collection of congener-specific data, since this type of analysis is likely to generate the most useful information for managing risks associated with PBDEs.

APPENDIX C

RESPONSES TO COMMENTS FROM THE BROMINE SCIENCE AND ENVIRONMENTAL FORUM

This appendix was prepared in response to the comments provided by the Bromine Science and Environmental Forum (BSEF). These responses focus on the comments in Appendix I and Appendix II of the document submitted by the BSEF. The MDEQ responses presented here are grouped into the same sections as identified in the BSEF comments. The specific BSEF comments (Appendix I and II only) can be found in Appendix D of this report.

Potential for Environmental Debromination

Deca-BDE has been measured in various media throughout the world and is often the dominant congener found in dust, soil, sediment, and sludge. It has also been found in wildlife inhabiting terrestrial and aquatic habitats. Deca-BDE has been measured in many wildlife species including higher trophic levels such as bear and fox. Peregrine falcons have been shown to have high concentrations of Deca-BDE in their eggs. The presence of high concentrations of Deca-BDE in these animals suggests that PBDE can move up the food chain. The data also suggest that the terrestrial environment may be a source of Deca-BDE. The study by Sellestrom et al., (2005), reports that higher brominated PBDEs, including Deca-BDE, are bioavailable from soils and accumulate in earthworms. Analyses of concentrations of BDEs in earthworms suggested debromination of Deca-BDE. Levels in earthworms present an exposure pathway into the terrestrial food web.

Several specific comments were presented by the BSEF regarding the potential for Deca-BDE to debrominate in the environment. The commenter stated that the evidence for environmental debromination of Deca-BDE is used by the TSG as the rationale for recommending the MDEQ support of a ban on Deca-BDE in Michigan. This one issue is not the sole reason for the recommendation, but rather contributes to the weight of evidence that Deca-BDE represents a significant environmental and public health concern and should be banned if a safer alternative is available. The other concerns include toxicity, exposure, bioavailability, and the identification of Deca-BDE in humans, fish, wildlife, and throughout the environment.

In general, the BSEF disagrees with the statement, “evidence is available which demonstrates that Deca-BDE debrominates to the more toxic PBDE congeners”. Specific examples are given in the TSG report, and more data have become available since the report was last released to show that under certain conditions, Deca-BDE may break down to lower brominated congeners in fish, animal models (e.g. rats), and in the environment. A recent review (Stapleton, 2006) concluded that Deca-BDE has the potential to debrominate in dust, soil, and sediment under environmentally relevant conditions. The PBDE congeners found in raptor eggs from China (Chen et al., 2007) and herring gull eggs from the Great Lakes region (Gauthier et al., 2007) provide evidence of Deca-BDE debromination. Recently published studies have found evidence of Deca-BDE debromination in fish living downstream from a

wastewater treatment plant (La Guardia et al., 2007) and an industrial park (Eljarrat et al., 2007). Evidence of debromination of Deca-BDE has also been found in sediments (Eljarrat et al., 2007).

He et al., (2006) found that Deca-BDE was debrominated by anaerobic bacterial cultures. It is true that some of the *in vitro* environmental fate data showing the microbial degradation of Deca-BDE may not be environmentally relevant. However, debromination of Deca-BDE in sewage sludge may be significant due to the large volumes of Deca-BDE present in sewage. Gerecke et al., (2005) used microflora from sewage sludge to examine the bacterial-mediated degradation of Deca-BDE. Their results indicated the debromination of Deca-BDE to Nona- and Octa-BDE congeners.

Photolytic degradation of Deca-BDE is dependent upon the substrate and the light source. The photolytic debromination of PBDEs bound to soil, sediment, and dust is most environmentally relevant. In the indoor environment, i.e. Deca-BDE bound to house dust, some ultraviolet light is blocked by glass windows and may not reach the indoor environment to a significant degree when windows are closed. However, car dust contains elevated levels of PBDEs and is susceptible to greater sunlight exposure resulting in more significant debromination. Degradation products from the photolysis of Deca-BDE are primarily the lower brominated congeners. When bound to soils, sediment, and house dust, the primary congeners formed from debromination are Hepta-, Octa-, and Nona-BDE congeners. These are all congeners found in the environment although not as extensively as the Tetra-, Penta-, and Hexa-BDEs (MDEQ, 2007).

Potential for Additivity

BSEF believes that the statement, "if the effects are additive, the risks could be significantly greater", is inappropriate for the following reasons: 1) the mechanism of action of PBDEs is unknown; 2) several *in vitro* studies indicate that some of the PBDE congeners have antagonistic activities; and 3) toxicity studies do not report similar effects for the various congeners. It is unclear which *in vitro* studies have shown that the various PBDE congeners have antagonistic activities. Some PBDE congeners have been shown to cause antagonistic effects with respect to the Ah receptor when co-treated with 2,3,7,8-TCDD. Since the mechanism by which the PBDEs cause adverse effects is unknown, it is unclear how this type of study would prove that PBDE congeners do not have additive effects. Furthermore, many of the PBDE congeners have been shown to cause similar effects on laboratory animals so the potential for congeners to enhance the toxic effects of each other cannot be discounted.

Potential for *in vivo* Metabolism to Lower Brominated Diphenyl Ethers (and Active Metabolic By-products)

As indicated in the BSEF's comments, one of the reasons the MDEQ recommends support of proposed legislation to ban Deca-BDE is because of its potential to be metabolized to biologically active metabolic by-products. Other reasons to support the legislation is that Deca-BDE has been shown to be biologically available based on detectable levels found in the tissues of various animals and humans and evidence that Deca-BDE is metabolized to more persistent, lower brominated congeners. Lastly, there is significant potential for humans to be exposed to Deca-BDE.

In general, BSEF believes that the evidence in the scientific literature regarding *in vivo* debromination of Deca-BDE is not convincing and that some of the more recently published studies have problems with study design and interpretation. The BSEF also states that some of the information, such as the high NOAELs reported in the NTP study (1986), does not support the speculation that toxic metabolites are produced from Deca-BDE.

The following recently published articles speak to the uptake, metabolism, accumulation, and distribution of Deca-BDE. These studies dispute many of the comments made by BSEF and provide additional justification to support proposed legislation to ban Deca-BDE.

Gomara et al., (2007) compared the levels of Deca-BDE in maternal serum, paternal serum, cord serum, breast milk, and placenta. BDE-47 was the predominant congener found in maternal, paternal, and cord serum, whereas Deca-BDE was the predominant congener in breast milk and placenta. Deca-BDE has also been found in breast milk in other studies (see PBDE Report). The volume of distribution can be affected by binding to proteins, biotransformation, rapid storage, or elimination.

Huwe and Smith (2007) dosed rats with Deca-BDE (0.3 ug/g in feed) for 21 days. They measured PBDE levels during a 21-day withdrawal period. PBDEs were measured in liver, GI tract, plasma, and carcass. The following BDEs accumulated in the rats and distributed proportionately throughout the body: Deca-BDE, three Nona-BDEs, four Octa-BDEs, and BDE-183 (a Hepta-BDE). Extensive metabolism of Deca-BDE was suggested with only 5% of the total dose present as parent compound after 21 days of exposure and < 4% in the feces. The presence of the lower brominated congeners at percentages higher than those present in the parent compound or spiked carcasses support the metabolic debromination of Deca-BDE. The concentration of Deca-BDE as well as the Nona- and Octa-BDEs in the liver of dosed rats was 2-3 times higher than those of the carcass, both on a whole weight and a lipid weight basis. Whole body half-lives were also determined for Deca-BDE and the lower brominated congeners. Half-lives varied by congener, although in general tended to increase with decreasing bromination. In cases where the data were fit to a biphasic decay curve, the elimination half-life was significantly longer than the distribution half-life. For Deca-BDE in plasma, the distribution half-life was 1.2 days, and the elimination half-life was 75.9 days. Two Octa-BDEs were found to increase in concentration after 21 days of withdrawal, which supports the potential for *in vivo* debromination of Deca-BDE to more persistent lipophilic congeners. The results of this study also indicate that absorption of Deca-BDE may be dose dependent, with greater absorption at lower doses.

Riu et al., (2007) force-fed pregnant Wister rats with [^{14}C]-Deca-BDE over 96 hours during gestation days 16-19. Deca-BDE was shown to be efficiently absorbed with more than 19% of the administered dose recovered in tissues and carcasses. The lowest concentrations of Deca-BDE residues were recorded for adipose tissue while the highest concentrations were found in the adrenals, ovaries, and liver. Most of the radioactivity was associated with parent compound however, biotransformation products accounted for 9-27% of the extractable radioactivity in adult tissues and 14% of that in the fetuses. Three Nona-BDEs and one Octa-BDE were identified; a hydroxylated Octa-BDE was isolated from the liver. The main metabolic pathways of Deca-BDE are debromination and oxidation. This study provided for the first time *in vivo* evidence for the presence of Deca-BDE and major biotransformation products in endocrine glands as well as in fetuses.

The fate of Hepta- to Deca-BDEs was studied in lactating cows exposed to a naturally contaminated diet by analyzing feed, feces, and milk samples from a previous mass balance study of PCB (Kierkegaard et al., 2007). Tissue distribution was studied in one cow slaughtered after the experiment. Deca-BDE was the dominant congener in feed, organs, adipose tissues, and feces but not in milk. Concentrations of Hepta- to Deca-BDEs in adipose tissue were 9-80 times higher than in milk fat, and the difference increased with increasing bromination. Metabolic debromination of Deca-BDE to BDE-207, 196, 197, and 182 was suggested. This study reports that meat rather than dairy products is the more important exposure route to higher brominated PBDEs.

Kunisue et al., (2008) investigated concentrations and patterns of brominated flame retardants including PBDEs in liver and adipose tissues of Japanese raccoon dogs. Relatively high concentrations of PBDEs were found in the livers. The liver to adipose tissue (L/A) ratio of Deca-BDE exceeded 1.0 in all the specimens suggesting hepatic retention of this compound. The results indicate that Japanese raccoon dogs accumulate Deca-BDE preferentially in blood-rich organs, probably due to their binding to proteins and/or rapid biotransformation as reported in rodents.

These recently published studies, along with those cited in the PBDE report which speak to the breakdown of Deca-BDE to biologically active metabolites in rodents and elevated levels of Octa- and Nona-congeners in the blood of workers exposed to Deca-BDE, provides one line of evidence for the MDEQ's concerns regarding Deca-BDE.

Margin of Exposure

In general, the MDEQ disagrees with the approach used by the BSEF for determining an MOE. The approach used by BSEF relies on a calculated human intake value for comparison to an experimental animal intake value. The MDEQ evaluated this approach and rejected it in favor of a total body lipid approach to estimate potential health risks of PBDEs. The total body lipid approach uses measured tissue concentrations in humans and compares these values to the tissue concentrations in animals that cause adverse effects. There are significant uncertainties in trying to back-calculate an estimated human intake value from human tissue concentrations. These include such things as limited knowledge regarding human exposures and insufficient data to quantify exposures, limited understanding of the pharmacokinetic properties of the chemical in humans, and uncertainty in accounting for human variability in all factors and properties. The use of measured human tissue concentrations to represent exposure and quantify potential risks bypasses the need for most of these data, since it represents an integrated exposure measure over time for all routes of exposure. The approach used by the MDEQ does have some uncertainty in estimating a rat tissue concentration from an experimental delivered dose however, this uncertainty is considerably less than back-calculating a delivered dose to humans using human tissue concentrations.

While the total body lipid approach for determining an MOE continues to be appropriate for lower brominated PBDEs, more recent data suggest some uncertainty for using this methodology for Deca-BDE. This information, as well as further comments on the BSEF risk assessment for Deca-BDE, is provided below.

One of the BSEF's specific comments was that it is inappropriate to use total body lipid for Deca-BDE because it has a limited volume of distribution. They stated that its systemic distribution is primarily restricted to the circulatory system and at most, the extracellular space. Based on this interpretation, the BSEF recommends that total body lipid should be substituted with the lipid fraction of whole blood or sera. The MDEQ disagrees that systemic distribution is restricted to the circulatory system and/or extracellular space. As stated below, several studies confirm wide tissue distribution of Deca-BDE. The MDEQ had identified in the 2007 draft report that the distribution of Deca-BDE to adipose tissue was a specific area of uncertainty with the MOE estimate for Deca-BDE.

Recent studies further confirm that Deca-BDE behaves differently *in vivo* than the lower brominated PBDE congeners. Deca-BDE is widely distributed throughout the body, whereas the lower brominated congeners are primarily distributed to lipids and adipose tissue. In the draft Toxicological Review of Decabromodiphenyl Ether (BDE-209) (U.S. EPA, 2006a) "Section 3.2 Distribution", the distribution of Deca-BDE is summarized as follows: "Collectively, these studies suggest wide tissue distribution, although relative distribution among various tissues differed across studies in adult rodents. Significant age-dependent differences in distribution to the undeveloped brain were noted."

Viberg et al., (2003) concluded that the highest concentrations of Deca-BDE were found in the plasma and the highly perfused tissues in mice after oral administration. Mouse brain, heart, and liver uptake levels of ^{14}C-labeled from Deca-BDE intake varied depending on the age of the animals with greater uptake and retention during PND 3 and PND 10, as compared to PND 19. Also, the levels of ^{14}C-labelled Deca-BDE found in the brains after dosing on PND 3 increased significantly over a seven day period after dosing, with peak levels at the time of rapid brain growth on PND 10. The results of this study suggest that the effects of Deca-BDE are induced by a metabolite or metabolites. The additional studies described above demonstrating increased levels of Octa-, Nona- and Hexa-BDE metabolites

after dosing or exposure to Deca-BDE in several animal species and human workers supports the suggested evidence that Deca-BDE effects may be induced by a metabolite(s). Although the Viberg et al., (2006) study demonstrated that Octa- and Nona-congeners also produce similar neurotoxic effects, it is not clear at this time the specific metabolite or combination of metabolites and/or parent compound that ultimately induces the neurotoxic effects following administered doses of Deca-BDE.

These recent studies in combination with Viberg et al., (2003), conflict with the BSEF's conclusion about the distribution of Deca-BDE. The most recent data also suggest the MDEQ's quantitative risk assessment presented in the 2007 PBDE report may not be appropriate for Deca-BDE. This approach included estimated body burdens based on the assumption that the total absorbed dose of Deca-BDE partitioned equally into the lipid compartment of the body. This approach is most appropriate for the lower brominated congeners which do distribute primarily to body lipids/adipose tissue. Deca-BDE is distributed primarily to the highly perfused tissues such as the adrenals, ovaries, and liver. In addition, it is not known at this time if the MOE evaluation should be conducted on the parent compound (Deca-BDE) and/or its metabolite(s). As a result, the risk assessment for Deca-BDE provided in the 2007 version of the report has been withdrawn from the final version (2008) of the report. More detailed information regarding the metabolism, distribution, and elimination of Deca-BDE, and a better understanding of the ultimate toxicant(s), is needed before a quantitative risk assessment with an acceptable level of uncertainty can be conducted.

Household Dust as an Exposure Pathway

Comments provided by BSEF did not alter the MDEQ's conclusion that household dust may be a significant exposure pathway. Regarding BSEF's comment specific to available data for children, the MDEQ agrees that PBDE levels reported in children from the U.S are very limited and noted this concern on page 88 of the May 2007 report. Published data support the finding that children ingest more soil and dust than adults due to their tendency to play on floors and on the ground outdoors along with their increased mouthing behaviors. Soil ingestion rates for younger children are greater than for adults and older children. The assumed soil and dust ingestion rates used in the Part 201 soil direct contact equation are 200 mg/day for young children and 100 mg/day for adults and older children (U.S. EPA, 1997; 2002). More recently, the U.S. EPA Child-specific Exposure Factors Handbook (External Review Draft) recommends 100 mg/day as the best estimate of the mean soil/dust ingestion rate for children under seven years of age based on soil and dust estimates. The recommended 95th percentile soil and dust ingestion rate for children is 400 mg/day (U.S. EPA, 2006). On a body weight basis and assuming 100 mg/day for an adult and 400 mg/day for a child, the soil and dust ingestion rate for a 10 kg child is approximately 30-fold greater than for a 70 kg adult. Several articles in the scientific literature discuss the concentrations of various contaminants in household dust.

Potential of Deca-BDE to Induce Developmental Neurotoxicity

The BSEF commented on the inadequacies of the two studies by Viberg et al., (2003 and 2007) as well as the 2007 study by Rice et al. The U.S. EPA (2006) also pointed out some of the problems with Viberg et al., (2003). Rice et al., (2007) and Viberg et al., (2007) were not reviewed by the U.S. EPA (2006). Although inadequacies of the Viberg et al., (2003) study were presented in the U.S. EPA document, other considerations were taken into account, and the U.S. EPA ultimately concluded that Viberg et al., (2003) was a critical study for development of an RfD for Deca-BDE. Some of the other considerations stated by the U.S. EPA include:

- Observation of effects following a single dose presents a significant concern regarding the potential neurotoxicity of Deca-BDE.

- Viberg et al., (2003) is a single dose study which may not be appropriate for development of an RfD. However, chronic exposures could also lead to developmental neurotoxicity via disruption of developmental events that take place during a critical window of development.

- Functional neurological effects observed following exposure during critical periods of development have been demonstrated with other PBDE congeners making the effects seen in Viberg et al., (2003) biologically plausible.

The U.S. EPA did not consider the limitations of Viberg et al., (2003) to be so significant that it was discounted. Since the Viberg et al., (2007) study was conducted in a similar manner, it is reasonable to assume that the U.S. EPA would reach the same conclusions regarding this study. The MDEQ typically relies heavily on toxicological determinations made by the U.S. EPA. Since there are no data published in the scientific literature to dispute the findings of the Viberg studies, the MDEQ maintains its decision to include them as evidence of neurodevelopmental toxicity from exposure to Deca-BDE.

In their review of the Viberg et al., study (2003), the BSEF combined the activity levels across all three time periods and only considered total activity. This treatment of the data is inappropriate and ignores an accepted measurement of neurotoxicity, which is motor activity habituation. A simple search of the National Library of Medicine's Developmental and Reproductive Toxicology Database identified 16 studies where motor activity habituation was used as a measurement of neurotoxicity.

Regarding the Rice et al., (2007) study, the BSEF concluded that no substantial effects were found on any of the parameters measured, even though the authors concluded that Deca-BDE produced developmental delays of the palpebral reflex in immature animals and altered the characteristics of spontaneous locomotor activity in adults similar to that seen in the Viberg et al., studies. The BSEF discounted these effects stating that the mild effects reported were transient, did not worsen with age, and did not persist into adulthood. A transient developmental effect is considered potentially significant.[1] As a matter of fact, the Viberg studies (2003 and 2007) demonstrated that the neurodevelopmental effects worsened with age, and the cholinergic effects seen in the 2007 study occurred in adulthood.

Another study (Viberg et al., 2008) has been published recently which contributes to the evidence that Deca-BDE is a neurodevelopmental toxicant. Three day old mice were given a single dose (20.1 mg)

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[1] Excerpt from EPA, Guidelines for Neurotoxicity Risk Assessment, April 1998

"Animal models of developmental neurotoxicity have been shown to be sensitive to several environmental agents known to produce developmental neurotoxicity in humans, including lead, ethanol, x-irradiation, methylmercury, and polychlorinated biphenyls (PCBs) (Kimmel et al., 1990; Needleman, 1990; Jacobson et al., 1985; Needleman, 1986). In many of these cases, functional deficits are observed at dose levels below those at which other indicators of developmental toxicity are evident or at minimally toxic doses in adults. Such effects may be transient, but generally are considered adverse. Developmental exposure to a chemical could result in transient or reversible effects observed during early development that could reemerge as the individual ages (Barone et al., 1995).

Comparisons of human and animal data for several agents known to cause developmental neurotoxicity in humans showed many similarities in effects (Kimmel et al., 1990). As evidenced primarily by observations in laboratory animals, comparisons at the level of functional category (sensory, motivational, cognitive, motor function, and social behavior) showed close agreement across species for the agents evaluated, even though the specific endpoints used to assess these functions varied considerably across species (Stanton and Spear, 1990). Thus, it can be assumed that developmental neurotoxicity effects in animal studies indicate the potential for altered neurobehavioral development in humans, although the specific types of developmental effects seen in experimental animal studies will not be the same as those that may be produced in humans. Therefore, when data suggesting adverse effects in developmental neurotoxicity studies are encountered for particular agents, they should be considered in the risk assessment process."

of Deca-BDE via a gastric tube. The brains from 1, 3, 7, 10, 14, and 28 day old mice were analyzed for certain brain proteins (CaMKII, CAP-43 and BDNF) that are important during the rapid brain growth and development of mammalian neonates. The results indicated that Deca-BDE does affect the levels of these important brain proteins thereby adding to the weight of evidence that Deca-BDE causes neurodevelopmental effects.

A substance shown to have effects in experimental animals is also assumed to cause those effects in humans. However, due to interspecies differences, the effects could be manifested in different and more significant ways in humans. Until studies are published in the scientific literature which adequately demonstrate that Deca-BDE is not a neurodevelopmental toxicant in humans, the studies cited above will remain in the report and be included as support for the reports conclusions and recommendations.

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APPENDIX D

COMMENTS SUBMITTED TO THE MDEQ

on

Polybrominated Diphenyl Ethers:
A Scientific Review
With Risk Characterization and Recommendations

May 18, 2007

Jim Sygo
Deputy Director
Michigan Department of Environmental Quality

Sent via email: levequel@michigan.gov

RE: Michigan Department of Environmental Quality's "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations," drafts dated January 2007 and May 2007

Dear Mr. Sygo:

The Bromine Science and Environmental Forum (BSEF) is a global industry association comprised of the major manufacturers of brominated and other flame retardants and our mission is to further the scientific understanding of our products.

BSEF has numerous concerns with the Michigan Department of Environmental Quality's (MDEQ) draft report, "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations." Attached to this transmittal message please find Appendices I and II, providing BSEF's detailed comments on the MDEQ's stated rationale for supporting a ban of Decabromodiphenyl ether (Deca-BDE) in the draft reports of January 2007 and May 2007, respectively; Appendix III: BFRIP IRIS Comments and Appendix IIIa: VCCEP DECA Exposure presentation; and Appendix IV: VCCEP Update Compiled.

Fundamentally, BSEF disagrees with the MDEQ's recommendation to support a ban of Deca-BDE based on the following:

1. Deca-BDE is clearly the most studied and analyzed flame retardant on the market. It has been rigorously evaluated and analyzed in the United States and Europe and has repeatedly been found safe for continued use;
2. The rationale for many MDEQ conclusions is incorrectly based on grouping all PBDEs together; and
3. Requiring the replacement of Deca-BDE without an in-depth analysis of the risks and benefits of moving to other flame retardants whose potential impacts on human health and the environment are far less understood is not sound public policy.

Deca-BDE is clearly the most studied and analyzed flame retardant on the market. It has been rigorously evaluated and analyzed in the United States and Europe and has repeatedly been found safe for continued use

Deca is the most studied flame retardant in history, including a 10-year-long risk assessment conducted by the European Union that examined 588 studies covering a wide range of potential human health and environmental concerns. That extensive study, concluded in 2004 and updated in 2005 and periodically since then, has not identified any human health or environmental risks in need of further regulation and

concludes that Deca-BDE is safe for continued use. That conclusion led directly to the decision by the European Commission to exempt Deca-BDE from its Regulation of Hazardous Substances Directive (RoHS) in October 2005. Deca-BDE has been exempted from key European Union regulatory programs and remains available for use in the EU. Sweden has implemented specific limitations on use, but it is anticipated that these will be lifted since they are not supported by EU risk assessments.

Other independent studies also confirm that Deca-BDE can be used in consumer products without concerns for health, including the U.S. National Academy of Sciences Review of DBDPO (Deca-BDE), the Consumer Product Safety Commission (CPSC) DBDPO Risk Assessment, the U.K. Department of Trade and Industry: Risks and Benefits in the Use of Flame Retardants, and the California Senate Office of Research report on PBDEs, among others.

The rationale for many MDEQ conclusions is incorrectly based on grouping all PBDEs together

It is misleading to refer to polybrominated diphenyl ethers (PBDEs) generically. Deca-BDE is a distinct product and evaluations and decisions regarding Deca-BDE should be specific to that product. Activists often refer to PBDEs as a group to create the perception of a larger concern when, in fact, two of the three PBDE products have not been in production or use for more than two years.

For example, the MDEQ's Executive Summary states, "PBDEs are of significant environmental concern because they are toxic, bioaccumulative, and persistent." In fact, Deca-BDE is not a persistent, bioaccumulative and toxic (PBT) substance. Deca is not classified as a PBT by the U.S. Environmental Protection Agency. Deca is persistent, which means it will be present in the consumer good throughout the life of that product, providing protection against fires, but Deca falls well below generally accepted bioaccumulation factors and is not toxic.

The MDEQ report also claims that "bills to ban or regulate products containing PBDEs have also been adopted in Hawaii, New York, Illinois, Maryland, Oregon, and Maine." No state has taken action against Deca-BDE, with the exception of a limited ban on the use of Deca in mattresses in the state of Washington. Some states have enacted prohibitions against Penta- and Octa-BDE, two other brominated flame retardants that are no longer produced, but not against Deca-BDE.

DecaBDE's hazard, risks and benefits should be derived from studies performed on and facts about the product itself. Deca's physical-chemical and toxicological properties are different from that of the former commercial penta- and octabromodiphenyl ether products. Assessing Deca on the basis of the congeners composing those former products is not valid.

Requiring the replacement of Deca-BDE without an in-depth analysis of the risks and benefits of moving to other flame retardants whose potential impacts on human health and the environment are far less understood is not sound public policy

MDEQ recommends that its support of a Deca-BDE ban is contingent upon the availability of a safe alternative and notes that, "The goal of removing PBDEs from commerce and reducing environmental levels needs to be accompanied with the use of alternatives proven to be safe for adequate fire protection and to assure the alternatives will not present unacceptable risks to public health or the environment. It is critical that the replacement chemicals be properly evaluated to ensure they will not become environmental contaminants of the future."

There is a wealth of data on Deca-BDE from more than ten years of studies – monitoring, biominoiting, emissions from the uses at downstream users, etc – and the results have consistently shown that there is no need for further risk reduction regarding the use of Deca. Suggesting that Deca be replaced by substances for which no such data exist actually rewards products for which there is very little data. It also carries the very real possibility of reducing fire safety, and potentially producing unintended or unforeseen environmental and human health impacts.

Alternatives to Deca-BDE are available, but principles of sound chemical regulation suggest that, in order to be considered "safer," an alternative should have been subjected to an equivalent battery of testing for human health and environmental effects as Deca-BDE and been found to have a more favorable toxicity profile. As such, for each application of Deca-BDe, any proposed alternatives should be identified and undergo a meaningful risk-benefit analysis before a ban is considered. In fact, no other flame retardant has been as exhaustively evaluated, from initial production through recycling at the end of consumer product life, and been found safe for continued use.

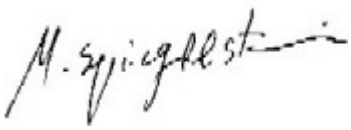
Any risk-benefit analysis must also take into consideration the potential impact on fire safety. DecaBDE's use as a flame retardant in products used in the home conveys a substantial benefit in reducing the very real risk of fire. In the U.S., fires in the home account for 82 percent of civilian fire deaths and 74 percent of the civilian fire injuries (An Overview of the U.S. Fire Problem, www.nfpa.org). Children under 5 and older adults face the highest risk of home fire death. One home structure fire was reported every 83 seconds. One civilian death occurred every 2 hours and 23 minutes (Karter 10/06). One civilian fire injury was reported every 29 minutes. In Michigan, 166, 149, 169, 161 and 141 persons died in fires in 2000, 2001, 2002, 2003, and 2004 according to the Office of the State Fire Marshal. The average annual fire loss (1976-2003) was $365,223,337.

The use of flame retardants in many consumer products is voluntary and is not required for most electronics, where Deca-BDE is most commonly used. Very few applications in which Deca-BDE is commonly used are guided by federal standards; only California has mandatory home furnishing requirements. In such high risk areas as furnishing, construction and wiring and cable, standards are controlled by building codes or State Fire Marshal regulations and vary greatly by state. Few are mandatory.

Conclusion

In closing, it is clear that banning Deca-BDE has the potential to directly decrease fire safety, and potentially increase the adverse impacts on the environment and human health. BSEF urges the MDEQ to review and carefully consider these comments before making any final recommendation that could lead the state of Michigan to take action against Deca-BDE.

Sincerely,



Michael C. Spiegelstein, Ph.D.
Chairman
Bromine Science and Environmental Forum

APPENDIX I:

BROMINE SCIENCE AND ENVIRONMENTAL FORUM (BSEF) COMMENTS

ON THE

MICHIGAN DEPARTMENT OF ENVIRONMENTAL QUALITY'S

DRAFT DOCUMENT

"POLYBROMINATED DIPHENYL ETHERS: A SCIENTIFIC REVIEW WITH RISK CHARACTERIZATION AND RECOMMENDATIONS"

DATED JANUARY 2007

April 26, 2007

SUMMARY

BSEF's comments are restricted to decabromodiphenyl ether (Deca-BDE), also known as BDE-209.

Deca-BDE's hazard, risks and benefits should be derived from studies performed on the product itself. Deca's physical-chemical and toxicological properties are different from that of the former commercial penta- and octabromodiphenyl ether products. Assessing Deca on the basis of the congeners composing those former products is not valid. For example, the U.S. Agency for Toxic Substances and Disease Registry (ATSDR) recently attempted a similar class review. Based on comments received from industry, ATSDR reviewed Deca separately from the lower brominated diphenyl ethers and derived a minimal risk level (MRL) of 10 mg/kg/d for intermediate-duration oral exposure (15-365 d) versus MRLs of 0.03 and 0.007 mg/kg/d for other PBDEs (Pohl and Bosch. 2005).

Pages 87 and 88 of the Michigan Department of Environmental Quality's (MDEQ) January 2007 draft report, "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations," provide the MDEQ's rationale for the recommendation to support legislation banning Deca-BDE, contingent on the availability of a safe alternative. BSEF's comments in this document are largely limited to those stated concerns.

In brief:

- MDEQ calculated MOEs for Deca-BDE using factors based on lower PBDEs. Correcting those factors for Deca results in MOEs of 483,173,077 (measured human sera level to calculated intake), 484,995 (calculated serum level to measured human level), 5,073 (400 mg dust ingestion), and 22,547 (100 mg dust ingestion). These MOEs are all substantially higher than the MOE (300) defined by MDEQ as indicating no risk.
- While dust may constitute a route of exposure, the exposure does not present a health hazard to humans, including children.
  - No correlation has been found between BDE-209 levels in house dust or indoor air and human plasma.
  - An MOE can be calculated using the reported BDE-209 indoor dust levels. Once again, the MOEs are very high, especially given the multiple layers of conservatism built into the calculations beginning with considering 20.1 mg/kg as a LOAEL based on Viberg et al and ending with basing the sera levels on a high dust level that is clearly an outlier.
- Several different *in vitro* studies indicate various PBDE congeners have *antagonist* activities for the same end point. Thus, making an assumption regarding additivity is speculation.
- There is no evidence that Deca-BDE debromination is a significant source of substances of concern in the environment:
  - Under artificial laboratory conditions, Deca can be forced to undergo degradation, but these conditions are not representative of real environmental conditions; and

- The substances formed in these lab experiments are different from what is typically found in the environment, indicating that what is found in the environment is not degraded Deca.

- Deca-BDE has been extensively tested at high doses for extended periods (NTP 1986). The results of the U.S. National Toxicology Program 14 and 90 day studies in rats and mice simply do not give rise to a plausible scenario under which Deca can be construed to produce "toxic" metabolites. In NTP's lifetime studies (e.g. two years), the NOAEL was at least 1,000 mg/kg/d in rats and mice. These very high NOAEL levels do not support speculation that toxic metabolites are produced.
- Evidence supporting Deca's metabolism to BDE47, 99, 100, 153 or 154, the PBDEs making up 90% of those found in human tissues, is either nonexistent or indicates very limited formation of perhaps one congener.

MARGIN OF EXPOSURE (MOE)

Page 87 of the MDEQ's January 2007 draft report, "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations," provides the following rationale for the recommendation to support legislation banning Deca-BDE: MDEQ states Deca-BDE's calculated MOE range from 400-400,000. The lowest MOE, 400, was based on MDEQ's determination of a LOAEL of 20.1 mg/kg for developmental neurotoxicity based on Viberg et al. 2003. The MOE of 400 was calculated as indicated on page 69, e.g. "Estimates of animal body burdens can be calculated from administered doses for comparison with reported human body burdens. The McDonald (2005) and the MDEQ TSG risk assessment use this body burden approach. In contrast, Hays and Pyatt (2006), estimate human intake levels from various exposure routes."

- According to Paustenback and Galbraith (2006), the term "body burden" is technically inaccurate, but is used to refer to the concentration of a given chemical in human tissues or the total amount of a chemical in the body.

- Hays and Pyatt (2006) utilized *measured* blood levels of BDE-209 in humans in their estimation of intake. Specifically, air and human blood levels were used to calculate an air:serum ratio which was then used in the exposure calculations. Similarly, measured PBDE blood and milk concentrations in humans were used to calculate a breast milk to serum ratio. Their "general exposure pathway" assessment was based specifically on *measured* serum concentrations of Deca reported in the literature. Further, for each of the 6 different exposure scenarios, Hays and Pyatt calculate a mid-range and upper estimate. The Hazard Quotients for these 6 exposure scenarios ranged from 0.0003 (Child>2-18 years, General Exposures, Mid-Range Estimate) to 0.2 (Infant, Mother involved in Formulation of Deca, Upper Estimate). None of the Hazard Quotients are indicative of risk.

- McDonald (2005) did not include BDE-209 in his assessment of PBDE daily intake. The BDEs included in his assessment were BDE47, 99, 100, 153 and 154, and according to McDonald "usually comprise more than 90% of the total PBDE body burden". If the 5 above-mentioned congeners currently comprise 90% of the PBDEs in the human body, then BDE-209 can at most contribute only 10% of the total. Further, the 5 PBDE isomers totaling 90% of the PBDE content in humans are components of the PentaBDE product. The PentaBDE product, along with the OctaBDE product, is no longer manufactured or sold, and once items currently in use are discarded from the home, these congeners will no longer have a direct source.

- MDEQ applied McDonald's approach to BDE-209 in Table 21 on page 71. McDonald calculated intake of the 5 PBDE congeners as follows:

$$\text{Intake (ng/kg/d)} = [(\ln 2) \times (\text{PBDE ug/kg}_{\text{lipid, measured}})] \times \frac{[(\text{Fraction adipose}) \times (1000 \text{ ng/ug})]}{[(\text{Half life d}) \times (\text{Fraction absorbed})]}.$$

  McDonald (2005) assumed the 5 PBDE congeners were equally distributed in the lipid fraction of serum, milk and adipose, and used the fraction of body weight that is adipose (0.3) in his intake estimate. This approach may be appropriate for these 5 congeners.

However, McDonald did not compare the content of the 5 congeners in each compartment individually; he only compared the total PBDE content in each compartment. Therefore his premise may or may not be accurate for each of these 5 congeners. For BDE-209, taking this approach is *known* to be incorrect. BDE-209 has a limited volume of distribution; its systemic distribution is primarily restricted to the circulatory system and at most, the extracellular space. Equal concentrations are not attained in blood, adipose or breast milk lipids. For example, Schecter et al. (2006) recently analyzed blood and breast milk collected from the same women. While blood and breast milk levels in each women for each of BDE47 (r^2 = 0.99), 99 (r^2 = 0.97), and 153 (r^2 = 0.96) were highly correlated, there was no correlation between blood and breast milk levels of BDE 183 (an octaBDE; r^2 = 0.02) and BDE-209 (r^2 = 0.19) (Fig. 1).[2] Therefore, one cannot utilize total body adipose to calculate intake or 'body burdens' of Deca-BDE. When using McDonald's formula to calculate Deca-BDE intake or 'body burden', the fraction of body weight that is adipose should be substituted by the fraction of whole blood or sera that is lipid. This is because the small fraction of the dose that is distributed systemically is confined nearly exclusively to the circulatory system.

Further, the data from Morck et al. (2003) actually indicates a much lower systemic absorption of BDE-209 than the widely cited 10% figure. Morck et al. collected bile from rats orally administered BDE-209, and reported that 10% of the dose was absorbed based on the BDE-209 detected in the bile. The fraction of the dose, ~0.10, detected in bile has been assumed by many to represent that absorbed. However, a substance's presence in the bile does not equate to systemic absorption. This is why systemic absorption is not determined by measuring levels in the bile.[3] In actuality, what Morck et al. reported was that fraction of the dose absorbed from gut into the liver (through which 100% of the blood flows after leaving the digestive tract) and transported directly to the bile without first undergoing systemic circulation. The levels in bile do not equate to that circulated throughout the body in blood. Blood is the media that transports substances to other tissues. The blood levels detected in the Morck et al. study and further reported in Sandholm et al. (2003) are indicative of a substance with very poor systemic distribution.

- The Viberg et al. 2003 and 2006 studies are widely cited as evidence that Deca-BDE is a developmental neurotoxicant. The studies were not conducted using accepted methodologies for determination of neurological effects. The manner in which results are presented in the publications – a series of bar graphs without data tabulation – makes it difficult for the reader to draw his/her own conclusions. Although published in peer-reviewed journals, the studies were poorly reported and poorly documented. Efforts by EU regulators, the U.S. EPA, the VCCEP peer consultation panel,

[2] Although Schecter et al. did not realize this, their results correspond to those of Takasuga et al. (2006). Takasuga et al. concluded lower brominated diphenyl ethers tended to transfer from mother's blood to milk, whereas octa- through decabromodiphenyl ethers did not transfer to milk to any significant extent. This is also consistent with the position taken in the VCCEP submission (2002) where we predicted BDE-209 would not transfer to any significant extent from blood to breast milk. The studies of Schecter et al. and Takasuga et al. support this conclusion.

[3] Systemic absorption is determined by comparing the area under the blood concentration versus time curve after intravenous and oral dosing. Intravenous dosing is considered to represent maximum (100%) absorption.

and industry to obtain further details regarding the study, especially the raw data, have been largely unsuccessful. For the purposes of review, activity counts were estimated from the bar graphs in the two publications in an effort to better understand the results (See Appendix II: BFRIP IRIS Comments). The resulting information yields little, if any, evidence of an effect due to treatment. Further, no evidence of an effect that worsens with age is seen. Viberg et al.'s results do not provide substantive evidence of a developmental neurotoxic effect due to Deca-BDE.

- For the purposes of this discussion, the intake of Deca-BDE (ng/kg/d) was calculated using McDonald's formula. The following variables were applied: 1) the highest measured BDE-209 blood level from Fischer et al. (2006), e.g. in the toddler, 233 ug/kg lipid; 2) McDonald's "fraction adipose" was substituted by the mean lipid content reported in the sera of the 4 individuals in Fisher's study (0.000385); 3) half life = 15 d as reported by Thuresson et al.; and 4) fraction absorbed as 0.10 as done by MDEQ. This calculation (see accompanying calculations) results in an intake by the toddler of 41.6 ng/kg/d. Using MDEQ's Margin of Safety (MOE) approach, the MOE between the calculated intake and a LOAEL of 20.1 mg/kg is 483,173,077. Thus, there is an ample margin of safety.

- Likewise, McDonald's formula can be used to back calculate blood levels in mice at MDEQ's LOAEL of 20.1 mg/kg. The intake in this case was 20,100,000 ng/kg. Assuming a total lipid content in blood of 3% (0.03) and a half-life of 1 day, whole blood levels in mice would be 96,681 ug/kg lipid. Calculated on serum lipid fraction of 0.000385, the concentration of Deca-BDE in sera following a 20.1 mg/kg dose would be 113,003,879. We can then compare these calculated blood levels to the highest measured concentrations in humans:

  Measured Human, Background: 233 ug/kg $lipid_{sera}$

  Calculated Human Intake Based on this blood level: 41.6 ng/kg/d

  MOE $_{\text{LOAEL to Calculated Intake}}$: 483,173,077

  Mouse

  Calculated Serum Level @ Intake = 20.1 mg/kg: 113,003,879 ug/kg $lipid_{sera}$

  MOE $_{\text{Calculated Serum Level to Measured Human}}$: 484,995

Clearly, the blood levels that might be achieved from a dose of 20.1 mg/kg in mice, grossly exceed the highest measured level in a human, in this case a toddler. Based on this, there is no indication of risk. The MOE between the calculated intake and a LOAEL of 20.1 mg/kg is 483,173,077. The MOE between the calculated blood levels at the LOAEL and the highest measured value in human

blood is 484,995. Surely, this represents an adequate safety factor such that all risks are insignificant.

Fig 1. Data extracted from Schecter et al. (2006) Toxicological and Environmental Chemistry 88(1-4):319-324.

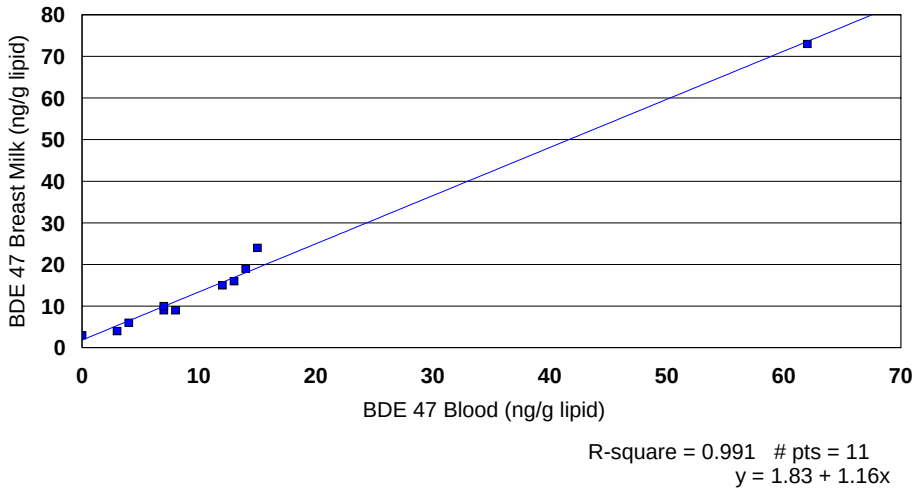
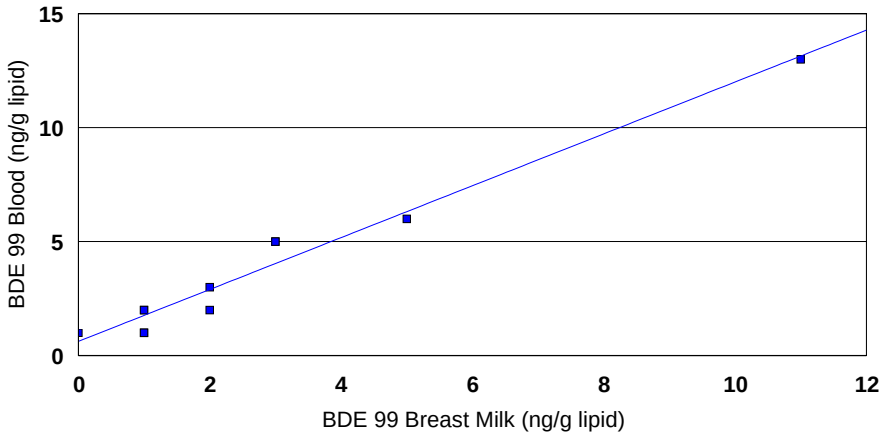
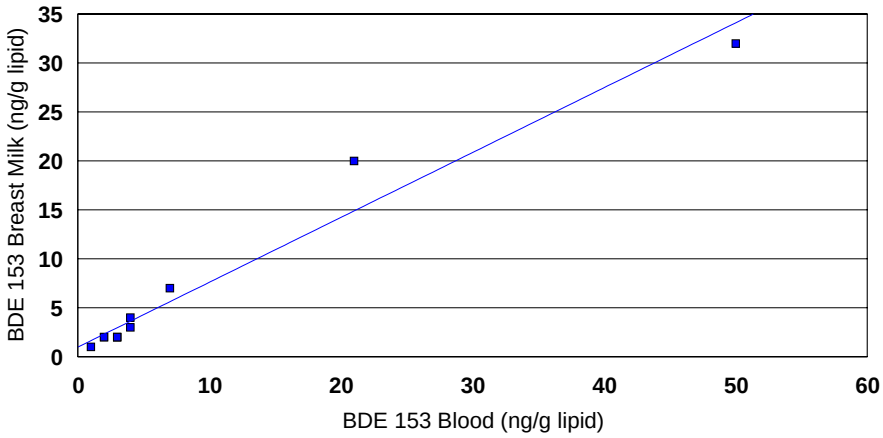


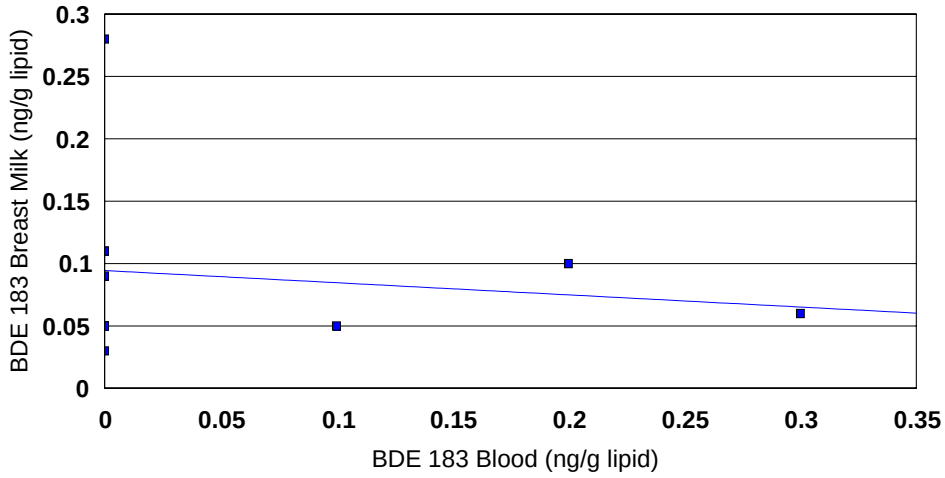
Fig 1., continued. Data extracted from Schecter et al. (2006) Toxicological and Environmental Chemistry 88(1-4):319-324.



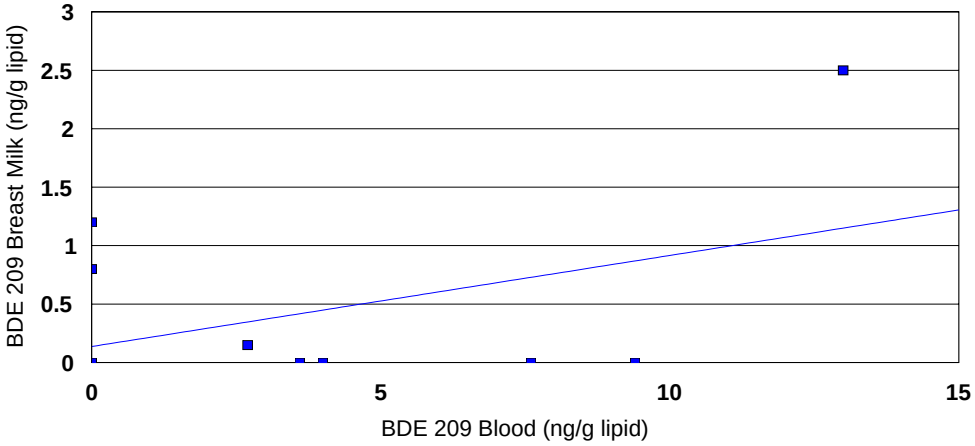
R-square = 0.967 # pts = 11
y = 0.624 + 1.14x



R-square = 0.963 # pts = 11
y = 0.976 + 0.663x



R-square = 0.0213 # pts = 11
y = 0.0944 + -0.0975x



R-square = 0.194 # pts = 11
y = 0.137 + 0.0779x

MOE Calculations

Intake (ng/kg/d) = [(ln2) x (BDE 209 ug/kg$_{lipid,}$ measured)] x $\frac{[(\text{Fraction Lipid}) \times (1000\ ng/ug)]}{[(\text{Half life d}) \times (\text{Fraction absorbed})]}$.

- Intake in Toddler calculated from a measured sera concentration of 233 ug/kg lipid:

  $$= (0.693)\ (233)\ \frac{(0.000385 \times 1000)}{(15)\ (0.1)}$$

  $$= 41.6\ ng/kg/d \text{ or } 4.16 \times 10^{-8}\ mg/kg/d$$

  - $MOE_{Toddler}$ at $LOAEL_{mice}$ of 20.1 mg/kg:

    $$= \frac{20.1\ mg/kg}{4.16 \times 10^{-8}\ mg/kg}$$

    $$= 483,173,076$$

- Back calculation of blood levels in mice at an intake of 20.1 mg/kg, t1/2 = 1 d, blood lipid = 3%:

  $$20,100,000\ ng/kg = (0.693)\ (BDE209_{blood}\ ug/kg\ lipid)\ \frac{(0.03 \times 1000)}{1 \times 0.1}$$

  $$= 96,681\ ug/kg\ lipid$$

- Back calculation of sera levels in mice at an intake of 20.1 mg/kg, t1/2 = 1 d, sera lipid = 0.000385:

  $$20,100,000\ ng/kg = (0.693)\ (BDE209_{sera}\ ug/kg\ lipid)\ \frac{(0.000385 \times 1000)}{1 \times 0.1}$$

  $$= 113,003,879\ ug/kg\ lipid$$

  - $MOE_{toddler} = \frac{113,003,879\ ug/kg\ lipid}{233\ ug/kg\ lipid}$

    $$= 484,995$$

HOUSEHOLD DUST AS AN EXPOSURE PATHWAY

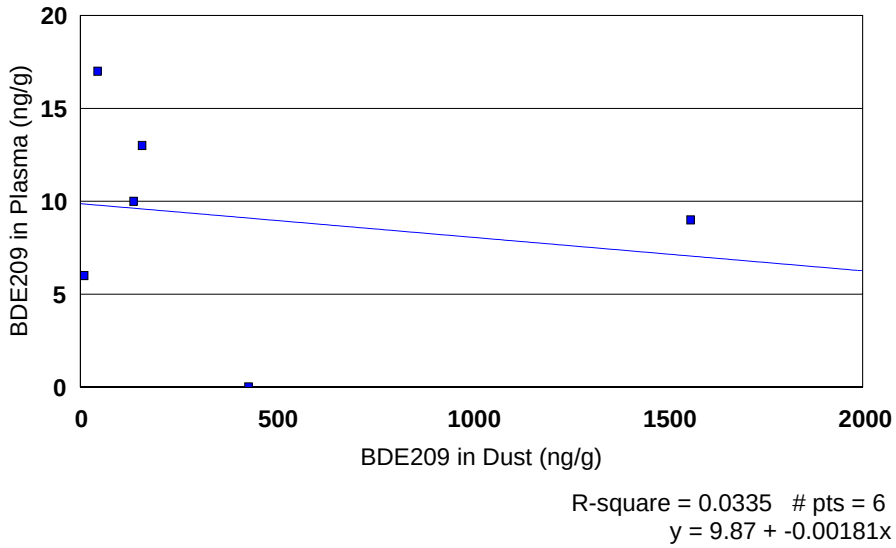
Page 88 of the MDEQ's January 2007 draft report, "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations," provides the following rationale for the recommendation to support legislation banning Deca-BDE: MDEQ states 1) levels of Deca-BDE are higher in children than adults based on 2 children in California, 2) household dusts contain high concentrations of PBDEs with BDE-209 typically as the most abundant congener, 3) children

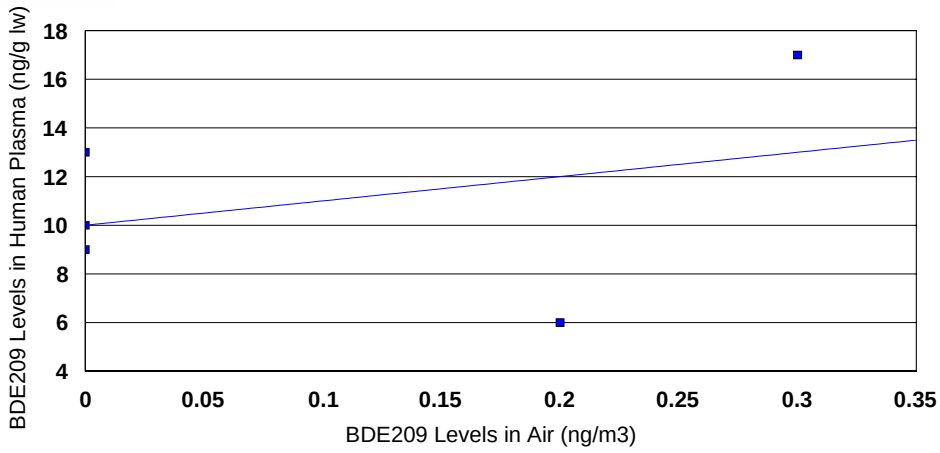
ingest more dust than adults, and 4) therefore, household dust may be a significant exposure pathway.

- An n of 2 is not an adequate sample on which to base a conclusion regarding all the children in the U.S. or in the state of Michigan.

- Karlsson et al. (2006) measured PBDE levels, including BDE-209, in human plasma, house dust, and indoor air (Fig. 2). No correlation was found between BDE-209 levels in house dust and human plasma. Similarly, no correlation was found between BDE-209 levels in indoor air and human plasma.

Figure 2. Data from Karlsson et al. (2006) regarding BDE-209 indoor air, dust, and plasma levels.





R-square = 0.114 # pts = 5
y = 10 + 10x

- Measured levels of BDE-209 in U.S. house dust are shown in Table 1.

Table 1. Reported Deca-BDE concentrations in North American indoor dust.

Literature Reference	No. Samples	Deca Dust Concentration (ng/g)		
		Range	Mean	Median
Stapleton et al 2005*	17	162 - 8,750	2,090	1,350
Schecter et al. 2005	9	143 – 65,777	8,567	665
EWG Study 2004	10	<400 – 7,510	2,394	Not Reported
Wilford et al. 2005	68	74 - 10,000	1,100	630
Morland et al. 2005	?	120 – 21,000	Not Reported	2,000
Hays and Pyatt 2006	5	917 – 1,475	Not Reported	Not Reported

*Stapleton et al. also reported Deca levels in 5 samples of dryer lint ranging from 58 – 2,890 ng/g.

- An MOE can be calculated using the reported U.S. BDE-209 indoor dust levels. The following assumptions were used: 1) a dust ingestion rate of 100-400 mg/d (MDEQ); 2) a body weight of 7.84 kg (0-2 yr) (Hays and Pyatt 2006); 3) serum lipid fraction of 0.000385 (Derived from Fisher et al. 2006); 4) a half-life in humans of 15 d (Thuresson et al. 2005); and 5) a BDE-209 dust content of 65,777 ng/g (highest reported U.S. concentration). At 0.066 mg BDE-209/g of dust, ingestion of 100 or 400 mg of dust would deliver 0.007 or 0.03 mg BDE-209, respectively. This would equate to an intake of 0.0009 or 0.004 mg/kg in a 7.84 kg child. Using McDonald's formula, these intakes would result in a BDE-209 serum lipid level of 5,073 (100 mg/d dust ingestion) or 22,547 (400 mg/d dust ingestion) ug/kg lipid. Comparing these calculated BDE-209 serum levels to those calculated after a dose of 20.1 mg/kg, results in MOEs of 22,276 (100 mg/d dust ingestion) or 5,012 (400 mg/d dust ingestion). Once again, the MOEs are very high especially given the multiple layers of conservatism built into the calculations beginning with considering 20.1 mg/kg as a LOAEL based on Viberg et al and ending with basing the sera levels on a high dust level that is clearly an outlier.

- Information presented during Deca-BDEs's peer consultation regarding dust as an exposure source, and the discussion in Hays et al. (2003) and Hays and Pyatt (2006) on this issue was not included in MDEQ's review.

  Hays et al. (2003) noted that decabromodiphenyl ether dust levels would have to exceed 7,000,000 ng/g of dust to equal the highest intake (3.9 $x10^{-1}$ mg/kg/d) estimated in the VCCEP's "general exposure pathway" that included intake from all possible sources. Decabromodiphenyl ether levels in indoor dust collected in North America, and reported in the literature after the VCCEP April 2003 Peer Consultation and the end of 2006 are presented in the table above. All of the reported concentrations are many orders of magnitude below that which would result in a human exposure equal to the highest VCCEP-estimated intake. That highest estimate intake in turn is orders of magnitude below the N.A.S.'s oral RfD, 4 mg/kg/d. This indicates that although dust may constitute a route of exposure to decabromodiphenyl ether, the exposure is inconsequential and does not present a health hazard to humans, including children.

POTENTIAL ADDITIVITY

Page 88 of the MDEQ's January 2007 draft report, "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations," provides the following rationale for the recommendation to support legislation banning Deca-BDE: MDEQ states "The MOE range of 400 – 400,000 for Deca-BDE does not take into account the potential additive effects of exposure to multiple PBDE congeners. If the effects are additive, the risks could be significantly greater."

- Deca-BDE's revised MOE are actually 483,173,077 (measured human sera level to calculated intake), 484,995 (calculated serum level to measured human level), 5,073 (400 mg dust ingestion), and 22,547 (100 mg dust ingestion). These MOEs are all substantially higher than the MOE indicating no risk, e.g. 300, as defined by the MDEQ.

- A concern for additive effects is only valid if the mechanism of action between compounds is the same. No mechanism of action has been defined for PBDEs.

- Several different *in vitro* studies indicate various PBDE congeners have *antagonist* activities for the same end point. Thus, making an assumption regarding additivity is speculation.

- The primary concern expressed by the MDEQ rests with developmental neurotoxicity based on studies by Viberg and Eriksson. These studies were performed using nonstandard test methods and were poorly reported and documented. (See comments on these studies in Appendix II: BFRIP IRIS Comments). Further, not even these studies report similar effects for all of the PBDE congeners tested. For example, the days of treatment on which effects were reported were different for BDE99 and 209.

The MDEQ reports a LOAEL of 20.1 and 0.06 mg/kg for BDE-209 and BDE99, respectively (See page 71, Table 21 of the Michigan report). The BDE-209 dose is 335 times that of BDE99, which suggests BDE-209 and 99 are not equi-potent. However, the endpoints producing these LOAELs are not the same for the two congeners, and thus such comparisons are not valid. In addition, if BDE-209 effects were additive to other PBDEs, its sera level would have to reach 113,003,879 ug/kg lipid prior to expressing any additivity. (This is the calculated mouse sera level at a LOAEL of 20.1 mg/kg.) This seems highly unlikely since the current MOE between this sera level and the highest measured human level is 484,995. And according to McDonald (2005), 5 BDE congeners not including BDE-209 comprise 90% of the PBDEs detected in humans. Thus, BDE-209 could at most contribute 10% to the total. Based on all of these considerations, concern regarding potential additivity of effects is misguided.

POTENTIAL FOR DEBROMINATION

Page 88 of the MDEQ's January 2007 draft report, "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations," provides the following rationale for the recommendation to support legislation banning Deca-BDE: The MDEQ states that "evidence is available which demonstrates that Deca-BDE debrominates to the more toxic PBDE congeners."

- The presence of Deca-BDE in the environment is predominantly in anaerobic sediment. When performing simulation biodegradation tests in anaerobic sediment, no significant degradation of Deca to lower BDEs was observed.
- Laboratory studies claiming degradation of Deca-BDE with specially cultivated bacteria, in sewage sludge, with chemical reducing agents, or via photolysis all share common features:
  - They do not reflect real environmental conditions; and
  - They do not observe degradation of Deca to the PBDEs found in the environment
- Were these processes to happen to any significant extent in the environment, then these congeners would be found in environmental samples in significant amounts.
- This is confirmed by a recent field study (all previous studies were carried out with Deca-BDE under laboratory conditions). This field study looked at potential photolysis of Deca in soil that had been amended with Deca-containing sewage sludge for many years. It did not find any indications for photolysis of Deca even under extreme conditions (Sellström 2005).
- Environmental monitoring studies confirm the above observations. Studies report no correlation between environmental Deca-BDE levels and environmental Penta-BDE levels in sediments in Europe and North America. If Deca were to degrade to Penta congeners to any significant extent, rising levels of Deca would not be accompanied by falling Penta levels
- Most degradation studies find that the degradation of Deca starts at a particular position of the Deca molecule, called the para-position. In a second step, often the second para-position is debrominated. The PBDEs typically found in the environment are brominated at that position. Since debromination of Deca seems to start at these particular positions, the environmentally relevant PBDEs cannot be coming from Deca degradation since they are brominated at these positions. Were they to come from that pathway, they would not have a bromine at those positions.
- A marker substance, specifically designed to indicate potential degradation of Deca-BDE has not been found in a large-scale environmental monitoring study in the EU.
  - In the EU the producers of Deca-BDE voluntarily carry out a large-scale 10-year environmental monitoring study for Deca-BDE. In order to account for potential degradation of Deca-BDE a specific marker congener was selected (BDE 126) that would be expected to be formed by degradation of Deca. This marker was discussed with the US EPA and agreed by the EU competent authorities. Initial results indicate that the marker was not detected, indicating no significant degradation of Deca-BDE.

POTENTIAL FOR *IN VIVO* METABOLISM TO LOWER BROMINATED DIPHENYL ETHERS

Page 88 of the MDEQ's January 2007 draft report, "Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations," provides the following rationale for the recommendation to support legislation banning Deca-BDE: MDEQ states "Although absorbed to a lesser degree and metabolized and excreted to a greater degree than the lower brominated congeners, there are some metabolic byproducts that may be biologically active."

- The early work on Deca-BDE in mammals indicated that rats did not absorb appreciable amounts from the diet (0.28-2% absorption depending on dose) (NTP 1986, El Dareer et al. 1987). Production of metabolites was limited, and was believed to occur mainly in the gut rather than systemically. Metabolites were not identified as lower brominated diphenyl ethers.

- Deca-BDE's poor absorption from the gastrointestinal tract is demonstrated in studies performed by the U.S. National Toxicology Program (NTP 1986; El Dareer et al. 1987), and Norris et al. (1973, 1975). NTP reported absorption of ~2 - 0.28% of the oral dose with the fraction absorbed declining with an increase in dietary dose. Following oral administration of ^{14}C-Deca-BDE, only trace levels of radioactivity were found in organs/tissues at any time point. The parent molecule (and all metabolites) was rapidly eliminated - > 99% of the dose was recovered in the feces and gut contents within 72 hours of oral dosing. *The overwhelming route and form of elimination was by fecal excretion as the parent molecule.* Less than 0.01% of the oral dose was excreted in the urine. Deca-BDE is capable of being metabolized if its absorption can be achieved; the parent molecule and 3 metabolites were detected in feces following oral or IV dosing of rats. The lower the dietary dose the lower the percent eliminated as metabolites, e.g. at a pretreatment dose of 277 ppm in the feed, approximately 2% of the dose was eliminated as metabolites. Thus, at environmental exposure levels, Deca-BDE is expected to be eliminated mainly as the parent molecule. The studies of Morck et al. (2003) and Sandholm et al. (2003), which appear to contradict these previous studies by reporting higher percent absorption and greater elimination as metabolites, suffer from interpretation and/or design flaws (See our comments on the Draft IRIS revision of Deca-BDE's RfD for details on these two studies).

- MDEQ raises the frequently expressed concern that Deca-BDE may contribute to exposure to lower brominated congeners via *in vivo* metabolism. This concern is not consistent with the research cited above. The primary evidence for this comes from feeding studies in fish (Kirkegaard et al. 1999, Stapleton et al. 2004, 2006). Over a 120 day period, trout absorbed approximately 0.005% of the 7.5 or 10 mg Deca/kg/d administered in their food (Kirkegarrd et al 1999). Uptake from food by carp at a dose of 940 ng/fish/d was immeasurable; the fish had no detectable Deca-BDE after consuming the treated food for 90 days *(*Stapleton et al. 2004; 2006*)*. Nevertheless, Stapleton estimated Deca's bioavailability in carp to be 0.4% of the dose based on detection of presumed metabolites. In neither of these fish studies were the lower brominated diphenyl ethers typically detected in wild fish, BDE-47, 99 and 100, identified as presumed metabolites, and Kierkegaard et al. concluded that "no evidence of debromination to these congeners was found in this study". Given its low

uptake, the metabolism of Deca-BDE in fish, irrespective of metabolite identity, is an insignificant source of lower brominated diphenyl ethers.

- Mörck et al. (2003) reported that, based on detection of test article-related substances in bile, rats absorbed up to 10% of Deca-BDE when administered in formulation specifically designed to enhance uptake. However, as noted previously in these comments, Morck et al.'s determination of 10% absorption via measuring Deca-BDE in bile has been erroneously interpreted as *systemic* absorption. The primary goal of the Mörck et al study was to determine the identity of Deca-BDE metabolites, and thus enhanced uptake was needed in order to maximize conditions for the formation of systemic metabolites (if any).

- Based on blood analysis, Morck et al. declared three nonabromodiphenyl ethers, which are typical impurities in the Deca-BDE product, and possibly hydroxy derivatives as putative metabolites. Brominated diphenyl ethers with less than nine bromine atoms were apparently not formed or were present in such small amounts as to be non-detectable.

- Nonetheless, Morck et al. (2003) reported that 65% of the dose was eliminated in the feces as metabolites. However, what Morck et al. reported as "metabolites" were not identified as products of Phase I or Phase II reactions, e.g. did not meet the accepted definition of a metabolite and were *not* identified as true biological metabolites produced by the rat or intestinal bacteria. In fact, these compounds were likely products of non-specific binding to proteins, lipids and other organic and inorganic matter in the gut. One of the papers referenced by Morck et al., Klasson Wehler et al. (1996), suggests this is the case. In that study, 2,2',4,4',5-pentachlorobiphenyl was said to be eliminated in the feces mainly as metabolites, "a large proportion of which were covalently bound to macromolecules and lipids". Sandholm et al. (2003) hints at this when saying that the phenolic "metabolites" could be "reversible binding to the thyroxin hormone transporting protein transthyretin" (see Sandholm's Discussion). Thus, Morck et al. defined anything other than the parent molecule, including nonspecific protein binding to serum proteins, as a "metabolite". Morck et al.'s unique definition is the reason that 65% of the dose was reported to be present in the feces as "metabolites". Thus, Morck's claim that 65% of the dose was eliminated in feces as 'metabolites' is incorrect.

- McDonald (2005) reports that ~90% of the total PBDEs detected in humans are BDE47, 99, 100, 153, and 154. It is difficult to understand how Deca-BDE has been construed to be a source of these congeners given a) its poor absorption, b) its rapid elimination and c) the lack of evidence indicating its metabolic conversion to these congeners. The congeners making up 90% of the total PBDEs in humans are associated with the former pentabromodiphenyl ether commercial product, not the Deca-BDE product. The simplest explanation of their origin is that they are derived from the pentabromodiphenyl ether product.

- MDEQ expresses a concern that "there are some metabolic byproducts that may be biologically active". Deca-BDE has been extensively tested at high doses for extended periods (NTP 1986). In NTP's 14-day studies, the NOAEL was 9,326 and 10,853 mg/kg/d in male and female rats, respectively, and 20,994 and 23,077 mg/kg/d in male and female

mice, respectively. In NTP's 90-day studies, the NOAEL was 3,066 and 3,994 mg/kg/d in male and female rats, respectively, and 10,233 and 11,566 mg/kg/d in male and female mice, respectively. In NTP's lifetime studies (e.g. two years), the NOAEL was at least 1,000 mg/kg/d in rats and mice. These very high NOAEL levels do not support speculation that toxic metabolites are produced. The results of the U.S. National Toxicology Program 14 and 90 day studies in rats and mice simply do not give rise to a plausible scenario under which decabromodiphenyl ether can be construed to produce "toxic" metabolites.

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APPENDIX II:

ADDENDUM TO

BROMINE SCIENCE AND ENVIRONMENTAL FORUM (BSEF) APRIL 26, 2007 COMMENTS ON MICHIGAN DEQ'S DRAFT DOCUMENT OF JANUARY 2007

"POLYBROMINATED DIPHENYL ETHERS: A SCIENTIFIC REVIEW WITH RISK CHARACTERIZATION AND RECOMMENDATIONS"

May 17, 2007

INTRODUCTION

Michigan DEQ issued a revised draft in May of 2007 of their January 2007 document titled "Polybrominated Diphenyl Ethers: A Scientific Review With Risk Characterization And Recommendations". The revised document does not appear to have considered industry's April 2007 comments (attached), which were limited to decabromodiphenyl ether. In addition, the revised document includes changes to decabromodiphenyl ether's effects assessment and margins of exposure. These changes were based on the publications of Viberg et al. (2007)[4] and Rice et al. (2007)[5]. This document provides industry's comments on those revisions.

POTENTIAL OF DECABROMODIPHENYL ETHER TO INDUCE DEVELOPMENTAL NEUROTOXICITY

Three studies investigating the potential for decabromodiphenyl ether to induce developmental nuerotoxicity have been published: Viberg et al. (2003)[6] (mice), Viberg et al. (2007) (rats), and Rice et al. (2007) (mice). Industry's assessment of these studies follows.

Viberg et al. (2003)

Viberg et al. (2003) reported on developmental neurotoxicity in mice. Male mice were administered a single dose of 2.2 or 20.1 mg BDE209/kg body weight by gavage on post natal day (PND) 3, 1.3, 13.4 or 20.1 mg/kg on PND10 or 2.2 or 20.1 mg/kg on PND19. BDE209 was dissolved in a mixture of egg lecithin and peanut oil and sonicated with water to yield a 20% fat emulsion vehicle. Control mice received the vehicle only. Spontaneous activity was measured when the pups, 10 mice from the 3-5 litters in each treatment group, were 2, 4 or 6 months old. Each treatment group contained pups from 3-5 liters; the total number of dams was not provided. Three measures of activity were recorded: locomotion (horizontal movement), rearing (vertical movement) and total activity (defined as all types of vibration within the cage). Motor activity was measured for a 60-minute period divided into three 20-minute spells. (This division into 3 20-minute segments appears arbitrary and the rationale for the division was not described in the publication.) The authors equated activity over time with behavior. Results were presented as a series of bar graphs. Additional pups (4-7 male offspring in each litter, with each age category composed of 2 litters) were gavaged with ^{14}C-BDE209 on PND 3, 10 or 19, sacrificed after 24 hr or 7 days, and ^{14}C-activity measured in brain, heart, and liver.

Viberg et al. concluded that as adults, neonatal mice treated on PND3, but not on PND 10 or 19, experienced a "disruption of habituation". Habituation was defined as a decrease in locomotion, rearing or total activity in response to the diminishing novelty of the test chamber over the 60 min test period. Control and BDE209-treated mice exposed on PND 10 and 19

[4] Viberg et al. 2007. Neurotoxicology 28(1):136-42.
[5] Rice et al. 2007. Neurotoxicol Teratol. 2007 Mar 27; [Epub ahead of print]
[6] Viberg et al. 2003. Toxicol Appl Pharmacol. 2003 Oct 15;192(2):95-106.

were said to exhibit habituation, whereas mice treated with 20.1 mg/kg on PND3 did not. The authors concluded that this disruption in habituation "worsened with age" by comparing activity in 2 month animals to 4 and 6 month-old animals (method of comparison was not described in the publication). ^{14}C-Activity in the brain was reported to increase with time post-dosing, and this finding was used as an explanation of why effects were found after treatment on PND3 but not on PND10.

The Viberg et al. (2003) publication does not provide vital information on many critical aspects of the study. A partial listing of this missing information includes: number of dams, number of sires, litter size, weight, etc, selection criteria used to reduce litter size, selection criteria of pups for assignment to treatment groups, numbers of pups from the same litter per treatment group (described simply as 3-5 litters per treatment group), which treatment group was composed of 3 litters and which composed of 4 or 5, stratification of treatment groups during activity testing – were animals from the control and treatment groups always tested concurrently so that environmental factors possibly affecting activity would affect all groups equally, were the activity tests run at the same time of day in the treated and control groups, what was the effect of collecting activity data for 20 minutes when EPA guidelines call for no longer than 10 minutes, etc. Very little information was included on the motion-measuring device, e.g. the Rat-O-Matic. As stated in the EPA guidelines: "Each device should be tested by standard procedures to ensure, to the extent possible, reliability of operation across devices and across days for any one device. In addition, treatment groups must be balanced across devices. Each animal should be tested individually. The test session should be long enough for motor activity to approach asymptotic levels by the last 20 percent of the session for nontreated control animals. All sessions should have the same duration. Treatment groups should be counter-balanced across test times. Activity counts should be collected in equal time periods of no greater than 10 minutes duration. Efforts should be made to ensure that variations in the test conditions are minimal and are not systematically related to treatment. Among the variables that can affect motor activity are sound level, size and shape of the test cage, temperature, relative humidity, light conditions, odors, use of home cage or novel test cage, and environmental distractions." Information of this type regarding the 'Rat-O-Matic' was not included in the Viberg et al. publication.

The Viberg study gives the appearance of three measurements of behavior, e.g. locomotion, rearing, and total activity. In reality, the same endpoint, motion, was monitored in three different ways simultaneously. Thus, Viberg's evidence for an effect is not as strong as implied. Further, the study's assessment of neurotoxicity was limited to one parameter – motion. In contrast, the OPPTS Guideline 870.6300 for the conduct of a developmental neurotoxicity study calls for the assessment of neurotoxicity via motor activity, response to auditory startle, assessment of learning, neuropathological evaluation, and brain weight, in three dose groups plus a control.[7] Viberg et al. utilized only 2 doses plus a control; thus, a dose-response pattern is not possible. Because of these and other deficits, the Viberg study

[7] Viberg et al. (2003, 2007) used two dose groups plus a control.

was not considered suitable for use in human health effects assessment under decabromodiphenyl ether's EU risk assessment.

Viberg's control and treatment groups were composed of 10 pups from 3-5 litters. The individual pups were apparently considered to independent from one another, and used for statistical comparisons. However, in developmental studies, the litter, rather than the individual pup, is considered the experimental unit for statistical comparisons. This is because littermates are more similar than non-littermates, and treating pups from the same litter as statistically independent will increase the false positive rate.

This is a fundamental flaw in Viberg's study. Littermates cannot be treated as independent observations – clearly pups in the same litter that are sired by one male and delivered from and raised by one dam are much more similar than pups sired by and raised by others. This similarity will affect the results. This is why developmental studies using multiparous species testing multiple pups per litter include the litter in the statistical model to guard against an inflated Type I (false positive) error rate. As a consequence, the U.S. EPA guideline for developmental neurotoxicity studies, OPPTS 870.6300, recommends at least *20 litters* per dose level so that at least 1 male and 1 female from each litter can used to generate test groups consisting of the required 10 males and 10 females per dose level.[8] For motor activity assessment, OPPTS 870.6300 requires examination of a minimum of 10 males and 10 females per dose group with each dose group made up of only 1 male and 1 female/litter. Viberg et al (2003), however, assessed motion in "a total of 10 mice were randomly picked from the three to five different litters in each treatment group". Therefore, Viberg's number of experimental units was 3-5/dose, in one sex only, compared to the requisite number of 10 animals/sex/dose from at least 20 litters in OPPTS 870.6300.

The statistical method also must account for the non-independence of any endpoint repeatedly measured in the same subject. Repeated measures were derived in the same subjects in this study.

The fact that each of Viberg's treatment groups contained two or more pups from the same litter also complicates the assertion that "effects worsened with age". Littermates are more alike than non-littermates and become more alike with age. Thus, any reported effect of treatment may simply be a reflection of similarities between littermates. Nonetheless, it is

[8] The same group of authors (Eriksson et al. 2005) has investigated this point and report in an *abstract* from the proceedings of the 2005 meeting of the Society of Toxicology, and basically validates their choice of using only 3-5 litters in their studies. The authors claim that randomly selected animals from at least 3 litters have the same statistical effect and power compared to litter-based studies in evaluating developmental neurotoxicity. This concept has not been accepted by the toxicology community at large or by any regulatory agency.

difficult to comprehend Viberg's assertion that effects worsened with age based on the data presented in the publication.

Viberg compared the number of movements between control and treated animals by time interval, e.g. treated animals' movements at 0-20 minutes compared to the control animals' movements at 0-20 minutes. This is only valid if control and treated animals were measured simultaneously at each time interval; the publication does not indicate whether control and treated animals were measured simultaneously. Nonetheless, the pattern of response is similar in the control and treated animals. Each dose group's movements declined over the 3 intervals as the novelty of their 'new' environment wore off and they stopped exploring. This is true for the controls as well as treated mice, and this basic behavior pattern was not altered by treatment (Table 1). Only the pattern's magnitude appears to differ. However, whether the magnitude is truly different is contingent on movements of the control and treated groups being recorded simultaneously with all other factors held equal. The materials and methods section of Viberg et al (2003) does not contain enough information about the conduct of this study to determine if this was the case. In fact, OPPTS 870.6300 requires "Treatment groups should be counter-balanced across test times."

"Total Activity" is likely the best overall indicator of motion because it was based on recording all types of vibrations within the cage, i.e., those caused by rat movements, shaking, grooming, etc. If the sum of the Total Activity (∑Total Activity; Table 1) is examined for mice at 2, 4, and 6 months, the values derived from the 3 groups are very similar. At 2 months of age, the ∑Total Activity over 0-60 minutes was 9900, 8700 and 8700 for the control, low and high dose groups, respectively. Likewise, at 4 months the values were 9900, 9900 and 9400 and at 6 months 10900, 10300 and 10800. These values do not appear substantially different, and do not support Viberg's contention that effects worsen with age.

Table 1. Activity counts estimated from figures reporting results in Viberg et al. (2003).

	Mice 2 mth			Mice 4 mths			Mice 6 mths		
	0	2	20	0	2	20	0	2	20
Locomotion									
0-20	600	500	390	600	580	350	630	600	380
20-40	300	200	200	280	200	230	300	240	300
40-60	50	50	130	50	50	200	50	50	250
∑+	850	750	720	930	830	780	980	890	930
Rearing									
0-20	2000	1500	300	2000	1600	300	2500	1800	200
20-40	500	600	310	500	500	310	600	800	210
40-60	100	0	280	50	50	300	50	50	210
∑+	2600	2100	890	2550	2150	910	3150	2650	620
Total Activity									
0-20	6000	4900	3900	5900	5900	4000	6000	6300	4000
20-40	3000	2900	2900	3000	2900	3000	3900	3000	3800
40-60	900	900	1900	1000	1100	2400	1000	1000	3000
∑+	9900	8700	8700	9900	9900	9400	10900	10300	10800
Mean Activity*									
0-20	2866	2780	1550	2833	2700	1550	2290	2900	1530
20-40	1280	1300	1150	1260	1200	1180	1600	1350	1440
40-60	350	350	770	370	400	1000	370	370	1150
Overall Mean** for 0-60 Minutes	1499	1477	1157	1488	1433	1243	1420	1540	1373

+Calculated for these comments to assist in evaluating the results by summing counts from 0-60 minutes.
*Calculated for these comments to assist in evaluating the results by taking the mean of the locomotion, rearing and total activity counts by time interval.

**Calculated for these comments to assist in evaluating the results by taking the mean of the "Mean Activity" at 0-20, 20-40 and 40-60 minutes.

Examined another way, the data also are suggestive of little effect of treatment and *improvement* with age (Table 2). For all parameters except rearing, activity counts in the treated group become closer to the control mean with age. And with the exception of rearing counts in the high dose group, the ∑Locomotion, ∑Rearing, and ∑Total Activity are 81-99% of that of the control value. Without knowledge of the standard deviation, it is impossible to know if a value of 81% of control is truly different or within the expected range.

It would appear highly precautionary to declare an effect of treatment based solely on the parameter of rearing, especially given that ∑Total Activity ranged from 88-95% of the control value, and therefore appears similar to the control value. To be recorded, mice would have to rear to height greater than some minimum. It is possible that mice in some groups did not rear to the same heights as other groups and thus total recorded rears may have been lower simply due to height. Even if real, it is not known if an effect on rearing (either total number or height) translates into neurological effects in humans or animals. Based on this analysis alone, Viberg et al.'s conclusion that decabromodiphenyl ether induced behavioral effects that also worsened with age is questionable.

Table 2. Percentage of control values in treated groups (mice) using activity counts estimated from figures reporting results in Viberg et al. (2003) and shown in Table 1 of this report.

∑ Counts from 0-60 Minutes	% of Control Value								
	Mice 2 mths			Mice 4 mths			Mice 6 mths		
	0	2	20	0	2	20	0	2	20
∑ Locomotion	100%	88%	85%	100%	89%	84%	100%	91%	95%
∑ Rearing	100%	81%	34%	100%	84%	36%	100%	84%	20%
∑ Total Activity	100%	88%	88%	100%	100%	95%	100%	95%	99%
Overall Mean for 0-60 Minutes	100%	99%	77%	100%	96%	84%	100%	108%	97%

Viberg et al. (2007)

In 2007, Viberg et al. reported on another study in neonatal animals: rats treated with BDE 209. The study design was similar to that used in mice, and similar concerns are raised as expressed previously in this document. Three day-old pups were administered 6.7 or 20.1 mg BDE 209/kg bw by gavage in a mixture of egg lecithin, peanut oil and water sonicated to yield a 20% fat emulsion. Control pups were treated with the vehicle only. Spontaneous activity was measured at 2 months of age. "A total of 20 rats were picked from the 3 to 5 different litters in each treatment group." The authors claim 3-5 litters will have the same statistical effect and power as the minimum of 20 litters per treatment groups in EPA and OECD guidelines. (EPA guidelines also call for a minimum of 10 animals/sex/dose group.) Motor activity was measured for a 60-minute period, divided into 3-20 minute spells using a "Rat-O-Matic" device; whereas EPA guidelines calls for collection of activity counts over time periods no longer than 10 minutes duration, but long enough for the motor activity to approach asymptotic levels by the last 20% of the session in the controls. Why data was collected for a 60-minute period was not explained in the Viberg publication. Immediately after testing, rats were given a single subcutaneous injection of nicotine (80 ug/kg bw) and returned to the test chamber. Activity was again monitored for 60 minutes.

Viberg et al. (2006) reported that no clinical signs of toxicity or effects on body weight occurred, but that spontaneous behavior (based on number of movements over time) and the cholinergic system (based on response to nicotine) in adult rats was affected. The effect on behavior was termed to be non-habituation.

Like their study in neonatal mice, Viberg et al. (2007) did not report whether treatment groups were balanced across time. If not, comparing treatment groups by time interval is not appropriate as external factors affect activity counts. Using ∑Total Activity as the most probable best indicator of motor activity, the results in rats at 2 months of age appear similar across treatments, e.g. 16500, 19900 and 18300 in the control, low and high dose groups, respectively (Table 3). In 2-month old rats injected with either saline or nicotine, the ∑Total Activity in the control-saline group (6000) is very similar to that in the 20 mg BDE209/kg-nicotine group (5500) whereas the control-nicotine and the 7 mg BDE209/kg nicotine group are similar. An increase in motor activity after nicotine injection would be expected, and was reported in the control-nicotine (10900) and 7 mg BDE209/kg-nicotine (13700) groups. However, this was not the effect observed in the 20 mg BDE209/kg-nicotine group. The ∑Total Activity in the 20 mg

BDE209/kg-nicotine group (5500) is very similar to that of the saline control group (6000). The data suggests that the 20 mg/kg-nicotine group did not receive an injection of nicotine.

Examination of the data using percent response of control values suggests little if any effect of treatment with decabromodiphenyl ether (Table 4). As with mice, activity in two decabromodiphenyl ether groups was similar to that in the controls at 2 months of age with the exception of rearing. Rats treated with nicotine only or nicotine plus 7 mg/kg decabromodiphenyl ether on PND3 were more active than those given a saline injection. The magnitude of their response to nicotine was similar. The magnitude of the response of the 20 mg decabromodiphenyl ether group to nicotine was similar to that of the saline control group (except for rearing), but substantially lower than that of the nicotine control group. This raises the question of whether the rats in the 20 mg/kg decabromodiphenyl ether group actually received an injection of nicotine at 2 months of age. A failure to inject nicotine could easily explain the results and is more probable than an effect on the cholinergic system due to a single dose of decabromodiphenyl ether.

Implications. The Viberg et al. 2003 and 2007 studies are widely cited as evidence that decabromodiphenyl ether is a developmental neurotoxicant. The studies were not conducted using accepted methodologies for determination of neurological effects. The manner in which results are presented in the publications - a series of bar graphs without data tabulation – makes it difficult for the reader to draw his/her own conclusions. Although published in peer-reviewed journals, the studies were poorly reported and poorly documented. Efforts by EU regulators, the U.S. EPA, the VCCEP peer consultation panel, and industry to obtain further details regarding the study, especially the raw data, have been largely unsuccessful. For the purposes of this review, activity counts were estimated from the bar graphs in the

Table 3. Activity counts estimated from figures reporting results in Viberg et al. (2006).

	Rat 2 mth			Rat 2 mths + Nicotine			
	0	7	20	0 + Saline	0 + Nicotine	7 + Nicotine	20 + Nicotine
Locomotion							
0-20	900	950	400	370	580	680	50
20-40	390	500	400	50	300	680	50
40-60	50	50	400	50	50	50	200
∑+	1340	1500	1200	470	930	1410	400
Rearing							
0-20	3000++	1500	400	650	1500	1500	50
20-40	1400	500	470	50	650	640	50
40-60	50	50	400	50	50	100	250
∑+	4450	2050	1270	750	2200	2340	350
Total Activity							
0-20	10000	11000	6000	3200	6700	9000	1400
20-40	4700	7000	6000	1400	3000	3300	1400
40-60	1800	1900	6300	1400	1200	1400	2700
∑+	16500	19900	18300	6000	10900	13700	5500
Mean Activity*							
0-20	4633	4483	2266	1407	2927	3727	500
20-40	2163	2666	2390	500	1317	1540	500
40-60	633	666	2366	500	433	517	1050
Overall Mean**	2476	2605	2341	802	1559	1928	683

+Calculated for these comments to assist in evaluating the results by summing counts from 0-60 minutes.
++This value appears abnormally high. As a consequence, the data in this group is skewed.
*Calculated for these comments to assist in evaluating the results by taking the mean of the locomotion, rearing and total activity counts by time interval.
**Calculated for these comments to assist in evaluating the results by taking the mean of the "Mean Activity" at 0-20, 20-40 and 40-60 minutes.

Table 4. Percentage of control values in treated groups (male rats) using activity counts estimated from figures reporting results in Viberg et al. (2006) and shown in Table 3 of this report. BDE209 doses = 0, 7 or 20 mg/kg bw.

∑ Activity	Rat 2 mth: % of Control Value			Rat 2 mths + Nicotine : % Control Value						
				0 + Saline	0 + Nicotine		7 + Nicotine		20 + Nicotine	
	0	7	20	Saline Control	Nicotine Rx To Saline Control	Nicotine Control	Nicotine Rx To Saline Control	BDE209 to Nicotine Control	Nicotine Rx To Saline Control	BDE209 to Nicotine Control
∑+ Locomotion	100%	112%	90%	100%	199%	100%	300%	152%	85%	43%
∑+ Rearing	100%	46%	29%	100%	293%	100%	312%	106%	47%	16%
∑+ Total Activity	100%	121%	111%	100%	182%	100%	228%	126%	92%	50%
∑Overall Mean**	100%	105%	95%	100%	194%	100%	240%	124%	86%	44%

two publications in an effort to better understand the results. The resulting information yields little, if any, evidence of an effect due to treatment. Further, no evidence of an effect that worsens with age is seen. Viberg et al.'s results do not provide substantive evidence of a developmental neurotoxic effect due to decabromodiphenyl ether. Nevertheless, due to the attention these studies have garnered, industry is sponsoring a developmental neurotoxicity study in rats. The study will be conducted according to OPPTS/OECD guidelines and under Good Laboratory Practices.

Rice et al. (2007)

Rice et al. (2007), in a manuscript accepted for publication, report on the effects of repeated doses decabromodiphenyl ether in neonatal mice. C57BL6/J mice were administered 0, 6 or 20 mg decabromodiphenyl ether/kg bw by placing small amounts of the dosing solution in each pup's mouth on PND2-15. The groups were composed of 11, 13 and 11 litters, respectively, of 3 male and 3 female pups each. The gavage vehicle was a 1:10 egg lecithin:peanut oil mixture that was sonicated and hand shaken to a 20% emulsion in water, e.g. comparable to that used by Viberg et al. 2003. Body weight, anogenital distance, crown-rump length, age of pinnae detachment/incisor eruption/eye opening and puberty were recorded. A functional observational battery examining a series of home cage, reflexive and sensorimotor behaviors were developed. The FOB was conducted every-other-day from PND2-20 (only data from PND14 onward shown in the manuscript). Locomotor activity was examined at PND70 and at 1 year of age in one male-female pair per litter in two-hour activity sessions grouped in consecutive 15-min time blocks. (Different pairs were examined at PND70 and 1 year.) Serum T4 levels were determined on PND21.

Treatment with decabromodiphenyl ether did not affect the timing of pinnae detachment, incisor eruption, eye opening, vaginal opening or testes descent. A delay in acquisition of the palpebral reflex was reported on PND14, but by PND16 (one day after cessation of dosing on PND15) the exposed animals developed the mature response and group differences were no longer apparent. An equivocal effect on forelimb grip strength was reported in that no effect of treatment was seen when both sexes were analyzed together, but a delay in strength development was reported in high dose males at PND14-16 when analyzed separately. A subjective difference in struggling during handling was reported; however, examination of the bar graphs (Fig 3 of the manuscript) shows no apparent pattern. An effect on male locomotor activity (an increase) at PND70 was reported in males at the high dose, but not females at any dose. No effect in male activity at one year of age was reported. None of the figures in the manuscript indicate there were statistically significant differences between treated and control animals.

Examination of Fig 5 indicates that young adult males, treated and control, were substantially less active than females of the same age. For example, activity counts in the first 15 minute interval ranged from ~225-400 in males compared to approximately 550 in females. Activity in the young adult male controls appeared abnormally low. In that respect, the young adult male previously treated with 20 mg decabromodiphenyl ether/kg bw actually appear closer to what would be expected than the controls.

Of importance is the fact that any mild effects reported were transient and did not "worsen with age" as reported by Viberg et al (2003) in their study. Further, Viberg et al. (2003) reported

mice were 'hyperactive' during the later portion of the test period. Based on Figure 5 of the Rice et al. manuscript, no such effect is seen in this study.

In summary, no substantial effect was found on any of the parameters measured in this study. Any mild effects reported were transient, did not persist to adulthood, and did not worsen with age.

MARGIN OF EXPOSURE (MOE)

- Our April 2007 comments indicated a MOE of **483,173,076** between intake in a toddler needed to produce a measured human sera level of 233 ug/kg lipid (e.g. 4.16 x 10^{-8} mg/kg/d) and Michigan DEQ's LOAEL of 20.1 mg/kg. Using a LOAEL of 6.7 mg/kg, the MOE between the intake needed to achieve the highest measured human sera level and this new LOAEL is **161,057,692** (see the attached "Revised MOE Calculation using a LOAEL of 6.7 mg/kg").

- Similarly, our April 2007 comments indicates a MOE of **484,995** between sera levels which could be achieved in mice at an intake of 20.1 mg/kg and the highest measured human sera level (233 ug/kg lipid). Using a LOAEL of 6.7 mg/kg, the new MOE is **10,778**.

- Our April 2007 comments also included MOEs calculated from the highest reported BDE209 level measured in U.S. house dust (65,777 ng/g). The MOEs between sera levels achieved after consuming 100 or 400 mg of this dust and a LOAEL of 20.1 mg/kg were **22,276** and **5,012**. Using the highest U.S. median house dust level of 2,000 ng/g and a LOAEL of 6.7 the MOEs are **18,000,000,000** and **8,968,560,714** at ingestion rates of 100 or 400 mg dust/d, respectively. Using a LOAEL of 6.7 mg/kg, the MOEs to sera levels achieved after consuming 100 or 400 mg of dust containing 65,777 ng/g are **7,425** and **1,671**, respectively.

- These MOEs are not indicative of risk.

LOAEL (mg/kg)	**MOE: Sera Levels**		**MOE: Dust Ingestion**			
	Intake at Highest Measured Human [Sera] vs. LOAEL	$[Sera]_{LOAEL}$ vs. Highest Measured Human	65,777 ng Deca/g dust		2,000 ng Deca/g dust	
			Dust Ingestion Rate (mg/d)		Dust Ingestion Rate (mg/d)	
			100	400	100	400
20.1	483,173,076	484,995	22,276	5,012	230,192,857	115,096,429
6.7	161,057,692	10,778	7,425	1,671	18,000,000,000	8,968,560,714

ADDITIVITY

- We refer to our comments of April 2007 on this topic. There is no evidence to suggest that effects are additive.
- In the event effects are demonstrated to be additive, at a LOAEL of 6.7 mg/kg, sera levels of BDE209 would have to reach 2,511,197 ug/kg lipid, e.g. rat sera levels at a dose of 6.7 mg/kg, prior to expressing any additivity. The highest reported BDE209 sera level in a human is 233 ug/kg lipid.

Revised MOE Calculations using a LOAEL of 6.7 mg/kg

Intake (ng/kg/d) = [(ln2) x (BDE 209 ug/kg$_{lipid,}$ measured)] x $\frac{[(\text{Fraction Lipid}) \times (1000 \text{ ng/ug})]}{[(\text{Half life d}) \times (\text{Fraction absorbed})]}$.

- Intake in Toddler calculated from a measured sera concentration of 233 ug/kg lipid:

  $$= (0.693)\ (233)\ \frac{(0.000385 \times 1000)}{(15)\ (0.1)}$$

  $$= 41.6 \text{ ng/kg/d} \quad \text{or} \quad 4.16 \times 10^{-8} \text{ mg/kg/d}$$

  - $MOE_{Toddler}$ at $LOAEL_{rat}$ of 6.7 mg/kg:

    $$= \frac{6.7 \text{ mg/kg}}{4.16 \times 10^{-8} \text{ mg/kg}}$$

    $$= 161{,}057{,}692$$

- Back calculation of blood levels in rats at an intake of 6.7 mg/kg, t1/2 = 1 d, blood lipid = 3%:

  $$6{,}700{,}000 \text{ ng/kg} = (0.693)\ (BDE209_{blood} \text{ ug/kg lipid})\ \frac{(0.03 \times 1000)}{1 \times 0.1}$$

  $$= 32{,}227 \text{ ug/kg lipid}$$

- Back calculation of sera levels in rats at an intake of 6.7 mg/kg, t1/2 = 1 d, sera lipid = 0.000385:

  $$6{,}700{,}000 \text{ ng/kg} = (0.693)\ (BDE209_{sera} \text{ ug/kg lipid})\ \frac{(0.000385 \times 1000)}{1 \times 0.1}$$

  $$= 2{,}511{,}197 \text{ ug/kg lipid}$$

  - $MOE_{toddler} = \frac{2{,}511{,}197 \text{ ug/kg lipid}}{233 \text{ ug/kg lipid}}$

    $$= 10{,}778$$

COMMENTS FROM THE U.S. EPA REGION V

Melissa Hulting/R5/USEPA/US

To Gilberto Alvarez/R5/USEPA/US@EPA; 05/16/2007 03:23 PM

TO	Todd Nettesheim/R5/USEPA/US@EPA, Al Alwan/R5/USEPA/US@EPA, David Macarus/R5/USEPA/US@EPA, Edward Smith/RTP/USEPA/US@EPA, Elizabeth Murphy/R5/USEPA/US@EPA
Subject	Re: Fw: Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations (Document link: Gilberto Alvarez)

Gilberto:

I was able to go through the document and I agree with Todd. The review is quite comprehensive--I thought they did a good job.

The State of Michigan should be aware that GLNPO has funded a study examining indoor concentrations of PBDEs in Michigan. Work is underway. The principal investigator is Dr. Stuart Batterman at the University of Michigan.

On pp. 38 and 39, concentrations of PBDEs in Great Lakes fish are discussed. More recent data for Great Lakes fish (GLNPO program) are in Streets et al. 2006 (ES&T 40:7263-69). Ron Hites also analyzed fish from the GLNPO fish contaminant program archive. That information is published in Zhu et al. 2004 (ES&T 38: 2779-84), which is cited on page 46 of the review, but is oddly not included earlier on p. 38.

Melissa
^^

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To Gilberto Alvarez/R5/USEPA/US@EPA; 05/10/2007 05:56 PM

cc: Al Alwan/R5/USEPA/US@EPA, David Macarus/R5/USEPA/US@EPA, Edward Smith/RTP/USEPA/US@EPA, Elizabeth Murphy/R5/USEPA/US@EPA, Melissa Hulting/R5/USEPA/US@EPA

Subject Re: Fw: Polybrominated Diphenyl Ethers: A Scientific Review with Risk Characterization and Recommendations (Document link: Melissa Hulting)

Hi Gilberto,

I was not able to perform a thorough review of the scientific review; however, my cursory review was quite favorable. I hesitated some providing the following suggestions because it is never easy preparing an extensive scientific report with new reports and publications being released monthly if not daily. But, I will provide the additional resources anyway because they may add to the weight of evidence.

(1) Washington State ban on deca-BDE.

(2) Report on Alternatives to the Flame Retardant DecaBDE: Evaluation of Toxicity, Availability, Affordability, and Fire Safety Issues (March 2007)
http://www.epa.state.il.us/reports/decabde-study/

(3) Li. et al 2006. Polybrominated Diphenyl Ethers in the Sediments of the Great Lakes. 4. Influencing Factors, Trends, and Implications. Environ. Sci. Technol., 40 (24), 7528 -7534.

Todd