

U.S. Environmental Protection Agency

Polybrominated
Diphenyl Ethers
(PBDEs)
Project Plan

March 2006

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A. INTRODUCTION

Polybrominated diphenyl ethers (PBDEs) are a group of brominated flame retardant chemicals of increasing interest to scientists, government agencies, and the public. These chemicals have been used in a variety of manufactured products, including foam cushioning used in furniture and plastics used in televisions and computers. In the event of a fire involving these products, PBDEs slow ignition and rate of fire growth, allowing more time for people to extinguish or escape the fire. However, findings that PBDEs are widely distributed in the environment and are present at increasing levels in people have raised concerns about the potential risks of PBDE exposure to human health and the environment.

This Project Plan provides a brief summary of relevant information on PBDEs, and outlines the U.S. Environmental Protection Agency's activities regarding PBDEs and related chemicals. In considering activities related to flame retardant chemicals, EPA will work with all interested parties to ensure that fire safety, environmental concerns and public health concerns are all taken into account. EPA will post this Project Plan and other materials related to PBDEs on its web site at www.epa.gov/oppt/pbde. The website will be periodically updated to report progress on the activities described in this Project Plan. EPA will use a variety of communications tools, including periodic updates to the website, to inform stakeholders and the public regarding progress on the activities described in this Project Plan.

B. BACKGROUND INFORMATION ON PBDEs

PBDE Congeners and Commercial Mixtures

PBDEs are a family of chemicals with a common structure of a brominated diphenyl ether molecule which may have anywhere from one to ten bromine atoms attached (Figure 1). Each individual PBDE variant, distinguished from others by both the number of bromine atoms and the placement of those atoms, is referred to as a congener. For example, there are 42 tetrabromodiphenyl ether congeners, each with four bromine atoms in different configurations. In theory, there could be as many as 209 PBDE congeners, but a much smaller number of congeners are commonly found in the commercial PBDE products and in measurements of PBDEs in humans and the environment (see Table 1).

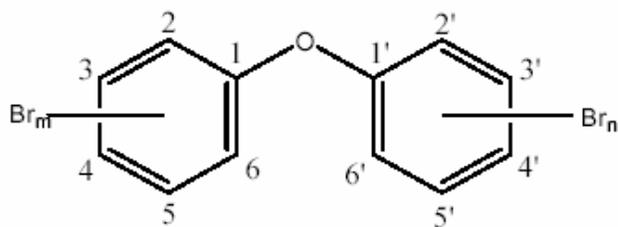


Figure 1. Generalized Structure of Polybrominated Diphenyl Ethers where (m+n) = 1 to 10 bromines

There are three types of commercial PBDE products, which are referred to as pentabromodiphenyl ether (pentaBDE), octabromodiphenyl ether (octaBDE), and decabromodiphenyl ether (decaBDE). Each of these commercial products, however, actually contains a mixture of various PBDE congeners (see Table 2). The leading commercial pentaBDE mixture, known as DE-71, is primarily comprised of tetraBDEs (especially BDE-47) and pentaBDEs (especially BDE-99 and BDE-100) – congeners with 4 or 5 bromine atoms – along with smaller quantities of hexaBDEs (BDE-153 and BDE-154, with 6 bromine atoms). The commercial octaBDE mixture is primarily comprised of heptaBDEs and octaBDEs (congeners with 7 or 8 bromine atoms) and also contains hexaBDEs and nonaBDEs (with 6 or 9 bromine atoms) along with small quantities of decaBDE (10 bromine atoms). The commercial decaBDE product is comprised almost entirely of the single fully-brominated congener, known as BDE-209, which has the maximum 10 bromine atoms. DecaBDE contains small quantities of nonaBDEs (congeners with 9 bromine atoms) as well.

TABLE 1. Selected PBDE Congeners

Congener	Number of Bromine Atoms	Chemical Name
BDE-28	3	2,4,4'-tribromodiphenyl ether
BDE-47	4	2,2',4,4'-tetrabromodiphenyl ether
BDE-85	5	2,2',3,4,4'-pentabromodiphenyl ether
BDE-99	5	2,2',4,4',5-pentabromodiphenyl ether
BDE-100	5	2,2',4,4',6-pentabromodiphenyl ether
BDE-153	6	2,2',4,4',5,5'-hexabromodiphenyl ether
BDE-154	6	2,2',4,4',5,6'-hexabromodiphenyl ether
BDE-183	7	2,2',3,4,4',5',6-heptabromodiphenyl ether
BDE-197	8	2,2',3,3',4,4',6,6'-octabromodiphenyl ether
BDE-206	9	2,2',3,3',4,4',5,5',6-nonabromodiphenyl ether
BDE-209	10	2,2',3,3',4,4',5,5',6,6'-decabromodiphenyl ether

A small number of the PBDE congeners are found most frequently, and in the greatest concentrations, in human and environmental samples. BDE-47 tends to be found more frequently than other congeners in measurements from humans, fish and other biota, followed by BDEs 99, 100, 153 and 154. In measurements of house dust, sediments, and indoor air, BDE-209 (decaBDE) seems to be dominant.

Uses of PBDEs

PBDEs and other flame retardant chemicals are used in certain products to reduce the risk of fire, particularly in items that are susceptible to igniting in fire situations, like furniture, or in which fires may start, like electrical devices. The commercial pentaBDE product is used almost entirely in flexible polyurethane foam in furniture, mattresses, carpet padding, and automobile seats. The commercial octaBDE product is used in acrylonitrile-butadiene-styrene (ABS) plastic that is used in certain electric and electronic devices. Commercial decaBDE is used primarily in high-impact polystyrene (HIPS) plastic that is frequently used to make the back part of television sets, and is also used in certain types of flame-retardant textiles. In recent years, almost all pentaBDE use has taken place in the Americas, while somewhat less than half of worldwide use of octaBDE and decaBDE has been in the Americas (see Table 2).

Concerns about PBDEs

In recent years, scientists have measured PBDEs in human adipose tissues, serum and breast milk, fish, birds, marine mammals, sediments, sludge, house dust, indoor and outdoor air, and supermarket foods. The mechanisms or pathways by which the PBDEs move into and through the environment and humans are not known, but are likely to include releases from manufacturing of the chemicals, manufacturing of products like plastics or textiles, aging and wear of products like sofas and electronics, and releases at the end of product life (disposal, recycling). In general, levels of PBDEs in humans and the environment are higher in North America than in other regions of the world, a finding that is often attributed to the greater use of pentaBDE in North America.

Studies have also been conducted in laboratory animals to gain a better understanding of the potential health risks of PBDEs. Studies of various commercial mixtures and individual congeners have suggested potential concerns about liver toxicity, thyroid toxicity, developmental toxicity, and developmental neurotoxicity. These findings raise particular concerns about potential risks to children. In addition, the presence of PBDEs in house dust and breast milk indicates that there are likely to be pathways of exposure to PBDEs that are of particular relevance for children. However, there remains much to learn about both exposure to PBDEs and the potential health effects; and there are different concerns for the different PBDEs.

A more detailed summary of the current scientific understanding of PBDEs is presented in Appendix A.

TABLE 2. Commercial PBDE Products

Commercial PBDE Product	Composition of Commercial Mixtures ¹	Uses	2001 Demand in Americas ² (metric tons)	Percentage of World Demand in Americas ²
pentaBDE (DE-71)	24-38% tetraBDEs 50-62% pentaBDEs 4-12% hexaBDEs 0-1% triBDEs	Flame retardant in flexible polyurethane foam for furniture, mattresses and carpet padding	7,100	95%
octaBDE (DE-79)	0.5% pentaBDEs 12% hexaBDEs 45% heptaBDEs 33% octaBDEs 10% nonaBDEs 0.7% decaBDE	Flame retardant in acrylonitrile-butadiene-styrene plastics used in computer casings	1,500	40%
decaBDE (DE-83R) (Saytex 102E)	0.3 – 3% nonaBDEs 97–99% decaBDE	Flame retardant in high impact polystyrene (HIPS) television set cabinet backs and commercial upholstery fabric	24,500	44%

¹Source of composition data is (Environ 2003) for pentaBDE, (ECB 2003) for octaBDE, and (WHO 1994) for decaBDE.

²Bromine Science and Environment Foundation estimates from www.bsef.com. In 2005, values for pentaBDE and octaBDE in the Americas were expected to go to zero.

Actions Regarding PBDE Production and Use

Increasing information on PBDEs in the environment has drawn the attention of policymakers at the international, national, state and local levels. In 2002, the European Parliament adopted a ban on marketing and use of pentaBDE and octaBDE throughout the European Union (EU). The ban went into effect in August 2004.

In July 2003, the State of California adopted a ban on the manufacture or distribution in commerce of any product containing pentaBDE or octaBDE. These restrictions are scheduled to take effect in 2006. Hawaii, Illinois, New York, Maine, Maryland, Michigan and Oregon have adopted laws similar to California's, and several other states are considering similar actions.

Great Lakes Chemical Corporation, the sole U.S. producer of the commercial pentaBDE and octaBDE mixtures, discontinued production of these two products in the U.S. at the end of 2004.

In general, decaBDE is not subject to the restrictions that have been adopted for pentaBDE and octaBDE. There is an EU regulation that will prohibit the use of certain chemicals in electric and electronic equipment as of July 2006. DecaBDE had been included on the list of chemicals that would be prohibited, but the EU granted an exemption for this chemical in October 2005.

Other international activities concerning PBDEs include an Arctic Council brominated flame retardants (BFRs) project and ongoing work by the BFRs Clearinghouse of the Organization for Economic Cooperation and Development (OECD). The Arctic Council is an inter-governmental forum addressing Arctic issues whose members include Canada, Denmark, Finland, Iceland, Norway, the Russian Federation, Sweden and the United States. EPA has been involved in the initial development of the Arctic Council's BFR-related activities, intends to continue involvement in their further development, implementation and tracking, and will provide technical expertise and other resources, where possible and as appropriate. The OECD is a forum where the governments of 30 market democracies work together to address the economic, social, environmental and governance challenges of the world economy. The OECD's BFR Clearinghouse has developed hazard/risk information fact sheets on the PBDEs, intends to update the fact sheets every 2-3 years, and will work to improve cooperation between producers and users of BFRs in order to reduce emissions to the environment.

More information on international activities is presented in Appendix B.

PBDE-Related Activities in the U.S. Federal Government

The U.S. federal government is playing a substantial role in research and assessment of PBDEs, and in taking appropriate management actions to respond to both scientific developments and developments in the market for PBDEs. A selection of federal government activities includes:

- EPA has proposed a Significant New Use Rule (SNUR) that would require prior notification to EPA by any manufacturer or importer intending to reintroduce pentaBDE or octaBDE in the U.S. The proposed rule would also provide EPA with authority to review the intended production or import of pentaBDE or octaBDE before it begins and to take actions to control potential risks as needed.
- EPA is leading a Furniture Flame Retardancy Partnership to evaluate alternatives to PBDEs in furniture applications. The partnership includes furniture and fabric manufacturers, chemical manufacturers and environmental organizations. Its focus has been assessment of alternatives to pentaBDE to inform decisions on adoption of substitutes.

- PentaBDE, octaBDE and decaBDE are being evaluated under EPA's Voluntary Children's Chemical Evaluation Program (VCCEP). Under VCCEP, PBDE manufacturers collect and develop exposure and health effects information on their chemicals, integrate that information in a risk assessment, and prepare a "data needs assessment." EPA has completed its Data Needs Decisions for the PBDEs and has requested that the PBDEs manufacturers develop additional data for assessing risks to children's health.
- As part of its National Lake Fish Tissue Study, EPA is measuring PBDEs in about 340 fish samples collected from 166 lakes and reservoirs. The statistical design of the study will allow EPA to develop the first national estimates of mean concentrations and distributions of PBDEs in fish.
- EPA is reviewing the available toxicology data and preparing toxicological profiles for tetraBDE, pentaBDE, hexaBDE and decaBDE congeners under its Integrated Risk Information System (IRIS) program.
- EPA is conducting and sponsoring a number of research activities to help develop a better understanding of releases, exposure and effects of PBDEs.
- A national survey of PBDEs body burdens in the U.S. population is being conducted by the Centers for Disease Control and Prevention (CDC), as part of the National Health and Nutrition Examination Survey (NHANES). PBDEs are being measured for the first time in this ongoing program, with survey data for 2003-2004 expected to be released in 2006.
- The U.S. Department of Agriculture is conducting studies of the absorption and metabolism of PBDEs in animals, and has also conducted measurements of PBDEs in meat and poultry.
- The U.S. Food and Drug Administration is conducting studies on methods for the analysis of PBDEs in different food and feed matrices, and has measured PBDEs in select fish samples.
- The National Toxicology Program (NTP) is conducting a subchronic toxicity study of the commercial pentaBDE mixture in laboratory animals, along with pharmacokinetic studies of three PBDE congeners.
- The National Institute of Standards and Technology is conducting studies on the emissions of PBDEs from plastics used in items such as computers and televisions.
- The U.S. Geological Survey is conducting studies on the presence of PBDEs in indoor environments and the migration of PBDEs from plastics in computers.

More information on federal government research and assessment of PBDEs is presented in Appendices C and D.

EPA's Project Plan for PBDEs

The cessation of pentaBDE and octaBDE manufacture in the U.S. is an important action that EPA believes will result in reduced amounts of these chemicals in the environment. However, the need for investigating exposures to and effects of PBDEs and related chemicals continues. In addition to changes in the market status of pentaBDE and octaBDE, forthcoming changes in furniture flammability requirements (being considered by the federal Consumer Product Safety Commission and the State of California) may increase demand for safer flame retardant chemicals and alternative means of achieving flame retardancy in products. This Project Plan identifies four key areas in which EPA is pursuing activities addressing concerns regarding PBDEs and other flame retardants. Many of these activities involve partnership and coordination with other federal agencies, industry and nongovernmental organizations.

EPA's four objectives are:

Objective 1: Assess Substitutes for Pentabromodiphenyl Ether and Octabromodiphenyl Ether. As U.S. manufacturers evaluate alternatives to pentaBDE and octaBDE, EPA is providing guidance on the potential hazards of alternative flame retardants. EPA is conducting a number of activities to identify, and to encourage development of, environmentally-preferable flame retardant chemicals and inherently flame retardant materials.

Objective 2: Assess and Evaluate Decabromodiphenyl Ether. EPA is pursuing a number of activities to help better understand the potential for human health and ecological risks from exposure to decaBDE and any breakdown products.

Objective 3: Assess Risks of Pentabromodiphenyl Ether and Octabromodiphenyl Ether. Although U.S. production of pentaBDE and octaBDE has been discontinued, the release of and exposure to these chemicals is likely to continue for an extended period of time, given their environmental persistence and the stocks of pentaBDE and octaBDE contained in existing furniture, electronic components and other products. EPA is therefore continuing to pursue an improved understanding of exposure to these chemicals and the associated hazards.

Objective 4: Track Developments Concerning Other Brominated Flame Retardants of Interest. In addition to the PBDEs, there are many other brominated flame retardants currently in use. EPA will track scientific developments regarding environmental levels, human exposure, and potential hazards.

C. KEY ACTIVITIES

Objective 1: Assess Substitutes for Pentabromodiphenyl Ether and Octabromodiphenyl Ether

The sole U.S. manufacturer of pentaBDE and octaBDE phased out production of these products at the end of 2004. Users of pentaBDE and octaBDE are currently evaluating and selecting alternative flame retardants to replace these chemicals.

For the flame-retarded polyurethane foam market, where pentaBDE has been a dominant product for many years, evaluation and selection of alternative flame retardants is a major undertaking. Foam and furniture manufacturers need to consider multiple factors in selecting flame retardants, including: compliance with flammability standards, cost of the flame retardant, compatibility with existing production equipment, costs of any necessary capital investments, ease of foam production, effect on important foam characteristics (such as durability, softness/firmness, and color), and possible health and environmental risks. The foam manufacturers are best situated to evaluate the cost and performance-related factors, with assistance from the chemical manufacturers who supply the flame retardants and the furniture manufacturers and other customers for the foam. However, the foam and furniture manufacturers are looking to scientific experts, including those at EPA, to provide guidance on the potential risks of alternative flame retardants.

There are similar issues related to identifying replacements for octaBDE in plastics. However, the transition to alternatives for octaBDE is expected to be less challenging than that for pentaBDE, because the volume of use of octaBDE is smaller and alternative flame retardants for use in similar applications are available.

Specific Activities

- 1.1 EPA has formed a Furniture Flame Retardancy Partnership with several industry associations and other stakeholders. The Partnership has conducted a screening level hazard assessment of flame retardant chemicals that may be suitable substitutes for pentaBDE. For each alternative chemical, the available scientific studies have been reviewed and summarized, data gaps identified, and environmental and human health effect endpoints characterized. This screening assessment was completed in September 2005 and is available at <http://www.epa.gov/opptintr/dfe/pubs/projects/flameret/index.htm>. The information in this report will help furniture manufacturers incorporate health and environmental considerations into their selection of replacements for pentaBDE.
- 1.2 EPA will work with the Furniture Flame Retardancy Partnership to review additional data on flame retardant chemicals used in furniture as appropriate.
- 1.3 EPA will monitor developments in the market for replacing octaBDE and will assess octaBDE substitutes if warranted.

Objective 2: Assess and Evaluate Decabromodiphenyl Ether

EPA will continue to evaluate two broad risk assessment issues for decaBDE. The first issue is the potential for human health and ecological risks from exposure to decaBDE itself. The second issue is the potential for breakdown or transformation of decaBDE in the environment, in organisms or from combustion of decaBDE containing products. Information regarding this issue is necessary for determining the relative importance of the breakdown or transformation products in the overall risk of decaBDE.

Specific Activities

- 2.1 EPA is conducting a review of the available toxicology data for decaBDE, and will update the decaBDE assessment in EPA's IRIS database. Completion of this assessment is projected for 2006.
- 2.2 EPA will monitor ongoing and planned research on the toxicity of decaBDE and its metabolites. Of particular interest are a developmental neurotoxicity study of decaBDE that is being sponsored by the European Union, and studies conducted by the FIRE project (Flame retardants Integrated Risk assessment for Endocrine effects; see www.rivm.nl/fire) in Europe. FIRE is conducting 28-day toxicity study in rats, and may follow this with other animal studies. EPA will coordinate with the EU and the FIRE project to ensure that all relevant information regarding decaBDE toxicology is shared in a timely manner.
- 2.3 EPA will further investigate the environmental fate and metabolism of decaBDE, including the potential for formation of lower-brominated congeners by debromination of decaBDE in the environment. Through its VCCEP program, EPA has determined that additional data are needed to address the potential of decaBDE to degrade to other substances in the environment. EPA will work with the industry sponsors of the decaBDE VCCEP assessment to address this data need.
- 2.4 EPA will prepare a white paper that reviews the available information on the environmental fate of decaBDE. The purpose of this paper is to assess the potential for debromination of decaBDE through various natural mechanisms (e.g. exposure to light, breakdown via metabolism in living organisms), the rate, extent and conditions under which debromination may occur, and whether debromination of decaBDE is likely to be a significant source of lower-brominated PBDEs in humans and wildlife. The white paper will also identify additional studies that would be helpful to developing a better understanding of the environmental fate of decaBDE. Emerging information currently under development and anticipated over the coming year will be an important part of this evaluation, including data needs identified through VCCEP. This effort will be initiated in 2006, and the white paper will be peer reviewed in accordance with

EPA's *Peer Review Handbook* and the Office of Management and Budget's *Final Information Quality Bulletin for Peer Review*.

- 2.5 EPA will conduct an interim review of all available scientific information concerning decaBDE in 2006/2007. The information to be considered in this review will include CDC NHANES data on decaBDE body burdens in the U.S. population, other studies reporting decaBDE body burdens in the U.S., data from EPA's National Lake Fish Tissue Study, the EPA White Paper on environmental fate of decaBDE, information developed under VCCEP, and other studies that may become available concerning decaBDE toxicology and environmental fate (including studies conducted or funded by EPA and other agencies listed in Appendices C and D). Based on this interim review, EPA will consider whether the information warrants pursuing additional research, risk assessment or regulation using existing legal authorities.
- 2.6 EPA is preparing to propose a SNUR under the Toxic Substances Control Act (TSCA) for flame retardants identified as candidates for use to meet the residential upholstered furniture flammability standards under consideration by the State of California and the U.S. Consumer Product Safety Commission (CPSC). Sixteen chemical substances/categories, including decaBDE, are being considered for inclusion in the SNUR. The SNUR would require persons who intend to manufacture, import, or process any of these chemical substances, or articles containing them, for use as a flame retardant in residential upholstered furniture to notify EPA at least 90 days before commencing such activity. The required notice would provide EPA with the opportunity to evaluate the intended use, and if necessary, to prohibit or limit such activity before it occurs.
- 2.7 EPA's Furniture Flame Retardancy Partnership is coordinating with the CPSC and will discuss whether to undertake a project to evaluate environmentally preferable fabric flame retardant chemicals, barrier technologies, inherently flame retardant materials and other fire safety approaches.

Objective 3: Assess Risks of Pentabromodiphenyl Ether and Octabromodiphenyl Ether

Production of pentaBDE and octaBDE in the U.S. was discontinued at the end of 2004. EPA has proposed a rule under TSCA that will provide it with the authority to review any new plans to manufacture or import pentaBDE and octaBDE. However, the release of and exposure to these chemicals is likely to continue for an extended period of time, given the stocks of pentaBDE and octaBDE contained in existing furniture, electronic components, and other products, and the persistence of these compounds. Debromination of decaBDE may also contribute to future exposures. In addition, it is possible that pentaBDE or octaBDE could be present in some products (furniture foam and plastics) imported into the U.S. EPA intends to investigate this issue further and seek further information on the presence of pentaBDE and octaBDE in imported articles. More

information on pathways of exposure to pentaBDE and octaBDE will help identify the types of activities that might be most effective in reducing exposure, if such activities are deemed necessary.

Specific Activities

- 3.1 In December 2004, EPA proposed a TSCA SNUR that would require prior notice to EPA from any entity planning to begin manufacture or import of pentaBDE or octaBDE, or any of the PBDE congeners that comprise these mixtures, for any use, after January 1, 2005. EPA plans to promulgate the SNUR in 2006. The SNUR will enable EPA to review any intended future manufacture or import of pentaBDE and octaBDE. Based on health or environmental concerns that may be identified during such a review, EPA could take actions to prohibit or limit the production, processing, distribution in commerce, use, and disposal of these chemicals.
- 3.2 EPA will prepare a white paper that reviews and synthesizes the available information on exposure pathways for PBDEs. The purpose of this paper is to address: first, the relative importance of different pathways of exposure (i.e. food vs. house dust vs. indoor air); and second, information on how PBDEs get into various exposure media (e.g., particular foods including fish, house dust, indoor air, sediments), including migration of PBDEs from products in use and releases from disposal or incineration of products. Information on current disposal and recycling practices for end-of-life products containing PBDEs will be collected. The white paper will also identify additional studies that would be helpful to developing a better understanding of exposure pathways for PBDEs. This effort will be initiated in 2006, and the white paper will be peer reviewed in accordance with EPA's *Peer Review Handbook* and the Office of Management and Budget's *Final Information Quality Bulletin for Peer Review*.
- 3.3 EPA is conducting a review of the available toxicology data for tetra-, penta- and hexaBDE congeners under its IRIS program. Completion of these assessments is projected for 2006.
- 3.4 Through its VCCEP program, EPA has identified additional toxicity information as a data need for both pentaBDE and octaBDE. Specifically, EPA has determined that the primary data needs are two generation reproductive toxicity studies for both pentaBDE and octaBDE. EPA will work with the industry sponsor of the pentaBDE and octaBDE VCCEP assessments to address these data needs. EPA will also seek further research on the toxicity of pentaBDE and octaBDE. Through these efforts, EPA will identify and prioritize proposed additional toxicology studies of individual PBDE congeners and/or PBDE mixtures common in human samples. EPA will consider developing a proposal for NTP to conduct a set of tests to better characterize the toxicology of several individual PBDE congeners.

3.5 EPA will conduct an interim review of all available scientific information concerning pentaBDE and octaBDE in 2006/2007. The information in this review will include CDC data on PBDE body burdens in the U.S. population, data from EPA's National Lake Fish Tissue Study, NTP studies of pentaBDE toxicology, and other studies that may become available concerning toxicology and environmental fate of PBDEs (including studies conducted or funded by EPA and other agencies listed in Appendices C and D). Based on this interim review, EPA will consider whether the information warrants pursuing additional activities, which could include:

- initiating further studies of exposure levels, exposure pathways, and/or toxicology of PBDEs.
- conducting a risk assessment of pentaBDE, octaBDE, or selected congeners. A risk assessment of these chemicals would include a review of the hazards, a dose-response evaluation, an exposure assessment, and a risk characterization.
- activities to reduce potential exposures to lower-brominated PBDE congeners.

Objective 4: Track Developments Concerning Other Brominated Flame Retardants of Interest

PBDEs are just one group of flame retardant chemicals currently in use in the U.S. The various flame retardants in use have different chemical and biological properties; therefore, each must be evaluated independently. In addition to PBDEs, there are two other brominated flame retardants in particular that have been measured in the environment and are the subject of continuing interest: tetrabromobisphenol A (TBBPA) and hexabromocyclododecane (HBCD). Another chemical of interest is decabromodiphenyl ethane, which has been used as a substitute for decaBDE in Europe and has been measured in environmental samples.

Specific Activities

4.1 Any new flame retardants not already in commerce in the U.S. must be submitted to EPA for a premanufacture review under TSCA. During the review period, EPA may take action to prohibit or limit the production, processing, distribution in commerce, use, and disposal of new chemical substances that raise health or environmental concerns. EPA will continue to scrutinize new flame retardants proposed for manufacture and import into the U.S. market and, where appropriate, will seek control measures and/or development of additional data on such chemicals by their manufacturers under TSCA Section 5 authorities.

- 4.2 EPA will monitor the developing science on brominated flame retardants, including TBBPA and HBCD. Among the important activities underway are studies of TBBPA and HBCD as part of the European Commission FIRE project. EPA will also monitor information on disposal and recycling practices for end-of-life consumer products containing flame retardant chemicals. EPA will review the available information on other brominated flame retardants in 2006/2007. Based on this review, EPA will consider whether the information warrants pursuing additional activities, which could include initiating additional studies of environmental fate, exposure pathways, and/or toxicology of certain flame retardant chemicals, and conducting IRIS assessments of hazard and dose-response, and/or full risk assessments of certain flame retardant chemicals.

D. CONCLUSION

This Project Plan identifies a number of activities that EPA is conducting regarding PBDEs, as well as activities it intends to initiate or consider within the next two years. Many of the activities are focused on identifying and prioritizing data needs and generating new information to help understand risks of PBDEs and other flame retardants.

As the activities outlined in the Project Plan proceed, EPA may identify and initiate additional activities that have not been defined at this time. EPA will evaluate use of additional voluntary approaches and its existing legal authorities, when necessary, to obtain additional information on potential releases, exposures, effects and risks of PBDEs and other flame retardants and to take actions to reduce potential risks, if deemed appropriate.

EPA will also continue to track activities and initiatives at the state and local level, as well as internationally, and will exchange technical information with other government agencies. In addition, EPA will maintain updated information on its PBDEs activities on its web site at www.epa.gov/oppt/pbde.

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APPENDIX A. CURRENT SCIENTIFIC UNDERSTANDING OF PBDEs

The scientific literature on PBDEs is growing at a rapid rate. This appendix presents a summary of the science on PBDEs as of early 2005. It is not meant to represent an exhaustive review and evaluation of the PBDEs literature. A detailed evaluation of studies or limitations of the available information is beyond the scope of this document, and this summary should not be taken to represent an assessment of the hazards or risks of PBDEs. EPA is currently conducting detailed assessments of the toxicological information for several PBDE congeners as part of its Integrated Risk Information System (IRIS) program. When completed, these assessments will provide a thorough review of the toxicological literature for tetra-, penta-, hexa- and decaBDE congeners.

PBDEs in the Environment and PBDE Exposures

PBDEs were first detected in the environment in 1979 (Alaee and Wenning 2002) and in biota in the 1980s (Jansson et al. 1987). Recent PBDE monitoring efforts suggest that several PBDE congeners are ubiquitous in the environment (NTP 2001) and that levels of PBDEs in sediment, air, wildlife, and human tissues are increasing. Measurements of PBDE congeners in humans, fish and other biota detect BDE-47 more frequently than other congeners. However, monitoring efforts have not analyzed collected samples for all possible PBDE congeners. Therefore, potential contributions of other congeners may have been overlooked.

SEDIMENT, SLUDGE AND EFFLUENT

PBDEs have been found in sediment samples, sewage effluent, and sewage sludge with differing congener profiles. Detailed analyses of sediment cores from Lake Superior detected decaBDE (BDE-209) in much greater concentrations than other PBDE congeners (Song et al. 2004). PBDEs found in sewage sludge and effluent may be a contributor to the PBDEs in sediment. TetraBDE, pentaBDE, and decaBDE congeners represent the majority of PBDEs found in a samples of Great Lakes sewage sludge (Hale et al. 2003) and in San Francisco Bay area sewage effluent and sludge (North 2004). The congener profiles in both studies indicate the largest portion of the total PBDE present in the sludge samples to be BDE-99. BDE-47 and BDE-209 are also dominant congeners in both studies. No explanation is available for the difference in congener profiles in sludge, effluent, and sediment. Potential regional differences in PBDE deposition and varying rates of congener breakdown in the environment may contribute to the differing congener profiles in these three media.

AIR AND INDOOR ENVIRONMENTS

PBDEs have been detected in ambient air and indoor environments (Harrad et al. 2004; Jaward et al. 2004; Lee et al. 2004; Shoeib et al. 2004; Wilford et al. 2004). Due to its low volatility and strong sorption to particulates, the deca congener BDE-209 is not thought to be a likely candidate for airborne transport (Hale et al. 2003); however, the majority of studies conducted to date have not analyzed outdoor air samples for BDE-209. Findings of BDE-209 in arctic biota suggest the possibility of long-range

distribution (Ikonomou et al. 2002; Wolkers et al. 2004). Indoor air samples contain a variety of tetraBDE, pentaBDE, and hexaBDE congeners (Harrad et al. 2004). The decaBDE congener, BDE-209, has been measured in outdoor and indoor window surfaces (Butt et al. 2004). In addition, tetraBDE, pentaBDE and decaBDE congeners are present in North American house dust (Rudel et al. 2003; Stapleton et al. 2005).

WILDLIFE

Numerous ecological studies provide convincing evidence that some PBDEs bioaccumulate (Hites et al. 2004; NTP 2001). Studies examining trends of PBDE levels in North American wildlife have found sharp increases over periods of 10-20 years, with PBDE levels doubling every 3-5 years. (Ikonomou et al. 2002; Lebeuf et al. 2004; Norstrom et al. 2002; Zhu and Hites 2004). Studies of Baltic Sea biota indicate that PBDE concentrations increase with the trophic level, suggesting biomagnification of PBDEs in aquatic ecosystems (Haglund et al. 1997; NTP 2001). New evidence suggests the breakdown of higher brominated congeners in fish and mammalian tissues, which may contribute to the accumulation of lower brominated congeners (Morck et al. 2003; Stapleton et al. 2004a; Stapleton et al. 2004b; Tomy et al. 2004). Bioaccumulation in a whale of methoxylated PBDEs, including methoxylated BDE-47, has been shown to be of natural origin and not from industrial sources. Several methoxylated-PBDEs are known natural products, and have been observed in dolphins and other marine mammals, sponges, algae, and acorn worms (Teuten et al. 2005). PBDE congener profiles in wildlife tissues are likely dependent on a combination of direct uptake from the environment, natural synthesis, debromination of higher brominated congeners to lower brominated congeners and differential biomagnification over trophic levels.

FOOD

Regional analyses have detected PBDEs in fish, meat, and dairy products (Hites 2004; Huwe et al. 2002; Ohta et al. 2002; Schechter et al. 2004). In fish and dairy products, BDE-47 appears to dominate the PBDE congener profile (Hites 2004; Ohta et al. 2002; Schechter et al. 2004) while BDE-99 is the dominant congener in meat (Huwe et al. 2002; Schechter et al. 2004). Detectable levels of BDE-209 are also found in many food samples (Schechter et al. 2004). In dairy samples, congener profiles indicate a wider variation than either fish or meat (Schechter et al. 2004). It should be noted, however, that the analyses of food items are currently limited to small numbers of samples from a limited number of locations.

HUMAN TISSUES

PBDEs have been found in human breast milk, adipose tissue, and blood samples (Hites 2004; Mazdai et al. 2003; Petreas et al. 2003; Schechter et al. 2003; She et al. 2002). Data for the U.S. are very limited at this time. BDE-47 appears to be the dominant congener in human tissues in the U.S.; however, the sample sizes have been very small and the inter-individual variability is great, most notably for BDE-47.

Most of the breast milk biomonitoring data have been generated in Sweden, although there are very limited data available for the U.S. and Canada. The largest breast milk study to date in the U.S. (Schechter et al. 2003) analyzed 47 individual breast milk samples

from nursing mothers in Texas. The levels in these volunteer women were markedly higher for all congeners than those that have been reported in Sweden and Finland (Meironyte et al. 1999; Meironyte Guvenius and Noren 2001; Meironyte Guvenius et al. 2003; Strandman et al. 2000).

In the U.S., limited data are available for PBDE levels in blood serum. However, compared to blood monitoring data from Sweden, Japan, and Norway, the most recent blood serum levels in U.S. populations are higher and quite variable. A recent retrospective time trend study of PBDEs in very small samples of blood serum in the U.S. has shown that median levels of the individual congeners as well as total PBDEs have increased in the U.S. from 1985 to 2002 (Sjodin et al. 2004). Data on PBDE blood serum levels in 12 maternal and fetal pairs from Indiana indicated that 6 PBDE congeners were measured in blood serum samples and that the predominant congener was BDE-47 (Mazdai et al. 2003). The range of total PBDEs in the maternal and fetal samples were very similar; however, the variability between the pairs was great, especially for BDE-47.

EXPOSURE PATHWAYS

As described above, PBDEs are present in many critical exposure media, including various foods, indoor air and house dust. However, the means by which humans and wildlife are exposed to PBDEs are not well understood. PBDEs may enter the environment in a variety of ways: release from manufacture of the PBDEs or of PBDE-containing products; release of PBDEs from products while they are in use; and release from products when disposed of or recycled. There are many uncertainties regarding the pathway of PBDEs from release to their presence in critical environments and exposure media. It is likely that the presence of PBDEs in indoor environments (house dust, indoor air, and indoor window surfaces) is in large part due to migration of PBDEs from products, including furniture and carpet foam and plastics in televisions and computers. Little is known about how PBDEs enter aquatic environments, and how they enter the food chain. The biomonitoring data described above indicate that there is human exposure to PBDEs; but the relative contributions of different exposure routes (such as inhalation, food ingestion, dust ingestion or dermal absorption) have not been characterized. The relative importance of these types of exposure may be different for infants, young children, older children, and adults.

Pharmacokinetic and Toxicity Profiles of PBDEs in Mammals

PHARMACOKINETICS

The available data indicate that the tetra congener BDE-47 and the penta congener BDE-99 are well absorbed and highly distributed to fatty tissues, such as adipose, adrenal glands, gastrointestinal tract, skin and liver (Hakk et al. 2002; Orn and Klasson-Wehler 1998; Staskal et al. 2005). Tetra- and pentaBDEs are slowly metabolized and slowly eliminated in rats (Hakk et al. 2002; Hakk and Letcher 2003). In mice BDE-47 (a tetraBDE) is also well absorbed and distributed, but it is effectively eliminated, with up to 81% of the dose excreted within 5 days (Staskal et al. 2005). DecaBDE is poorly

absorbed by rats, with more than 90% of the dose excreted within 2 days (Morck et al. 2003).

HEPATIC EFFECTS

Studies conducted in rodents have demonstrated hepatotoxic potential with exposure to PBDE mixtures. The spectrum of hepatic effects observed in studies of various PBDE congeners and mixtures includes microsomal enzyme induction, liver enlargement, and degenerative histopathologic alterations. In rodents, dietary exposure to 5-10 mg/kg/day (IRDC 1976; IRDC 1977; Norris et al. 1973; Norris et al. 1975; Zhou et al. 2001; Zhou et al. 2002) and 56 mg/kg/day (Carlson 1980) of PBDEs typically caused liver enlargement with or without degenerative changes, and the incidence and severity of effects were generally dose-related and more frequent and pronounced in males than females. Effects are generally more severe with commercial mixtures of octaBDE and pentaBDE than decaBDE (Carlson 1980; IRDC 1976; IRDC 1977; Norris et al. 1973; Norris et al. 1975; NTP 1986; WIL Research Laboratories 1984; Zhou et al. 2001; Zhou et al. 2002). Some of the studies indicating thyroid effects of decaBDE were conducted on older commercial mixtures that contained more impurities than the products currently manufactured.

When scientists began studying PBDEs, there was some expectation that the PBDEs might have some toxicological similarities to dioxins, due to the structural similarities of these chemicals. To test this hypothesis, scientists conducted studies of hepatic enzyme activity. Induction of the cytochrome P450 enzyme CYP1A is a well-established characteristic of chemicals that bind to the aryl hydrocarbon receptor (AhR), most notably dioxins, furans and co-planar PCBs (also known collectively as "dioxin-like compounds"). By binding to the AhR a chemical may initiate a number of other effects that characterize "dioxin-like" toxicity in addition to inducing CYP1A. Hence CYP1A induction is considered an indicator that a chemical can bind to the AhR and has the potential to cause toxicity similar to dioxin. Initial studies were conducted in commercial PBDE mixtures and have been reported to induce CYP1A at doses of 18 – 60 mg/kg (Hallgren et al 2001; Stoker et al. 2004). However, the tetra congener BDE-47 did not induce CYP1A at doses up to 100 mg/kg (Staskal et al. 2005). Studies in fish (see below) have also found CYP1A induction from commercial PBDE mixtures, but not for individual PBDE congeners. Given that there is no indication of CYP1A induction by PBDE congeners, this suggests that there is a constituent of the commercial mixtures, i.e. a contaminant other than the PBDE congeners, that is responsible for the enzyme induction. It appears that PBDEs themselves do not have dioxin-like activity.

IMMUNOLOGICAL EFFECTS

Disruption of normal immune function may result in an inability of the animal to respond to and recover from further stressors such as illness and disease. Short term (14-day) exposure to 18-72 mg/kg/day of commercial pentaBDE mixtures in mice resulted in suppressed antibody response, decreased thymus weight (Fowles et al. 1994) and decreased IgG immunoglobulin production (Thuvander and Darnerud 1999). Short-term exposure of mice to 18 mg/kg/day of BDE-47 caused significantly reduced numbers of total lymphocytes and splenocytes (Thuvander and Darnerud 1999). Chronic ingestion of decaBDE at 2240 mg/kg/day for 103 weeks caused splenic lesions in rats (NTP 1986).

No inhibition of the immune response system was observed in a study of the effect of BDE 85 (Fernlof et al. 1997). Currently available information is insufficient to adequately characterize the immunotoxic potential of PBDEs.

DEVELOPMENTAL AND NEUROBEHAVIORAL ALTERATIONS

Gestational exposure to 1000 mg/kg/day of decaBDE for 19 days resulted in increased early resorptions in rats; the authors concluded that these were of limited significance based on comparison to historical control data (Hardy et al. 2002).

Developmental neurotoxic effects have been found in rodent studies of exposure to individual PBDE congeners. In neonatal mice, postnatal day 10 was determined to be a critical window of sensitivity to PBDE exposure. Animals treated with 0.6 and 6 mg/kg/day of BDE-99 for 15 days (Branchi et al. 2002) and single 0.4 mg/kg doses of BDEs 47, 99, 153, or 209 (Birnbaum and Staskal 2004; Branchi et al. 2003; Eriksson et al. 2001; Viberg et al. 2002; Viberg et al. 2003a; Viberg et al. 2003b) showed neurobehavioral alterations, hyperactivity extending into adulthood, and a nonhabituating behavior profile. In male offspring of dams treated with single 60 µg/kg and 300 µg/kg doses of BDE-99, developmental reproductive and neurobehavioral landmarks were significantly delayed (Kuriyama et al. 2005). Developmental reproductive effects have also been observed following 31 days of exposure to 30 mg/kg/day and 60 mg/kg/day of the commercial pentaBDE mixture (Stoker et al. 2004).

ENDOCRINE DISRUPTING EFFECTS

Evidence from experimental animal studies for certain PBDE congeners and commercial mixtures has indicated the potential for effects on the thyroid system. Thyroid effects include reduced serum levels of the thyroid hormone T₄ (thyroxine) with exposure to commercial pentaBDE at doses of 3 mg/kg/day (Stoker et al. 2004), 10 mg/kg/day (Zhou et al. 2001; Zhou et al. 2002), and single acute doses of 0.8 mg/kg and greater (Fowles et al. 1994). In addition, follicular cell hyperplasia, which is a sign of disrupted thyroid function, was observed in male mice orally exposed to 3200 mg/kg/day or more of decaBDE (NTP 1986). Disruptions in maternal and fetal thyroid homeostasis can result in neurologic impairment, including developmental delays and decreased IQ in children of mothers with small reductions in T₄ (Haddow et al. 1999; Pop et al. 1999; Pop et al. 2003).

Hydroxylated BDEs, which are metabolites of PBDEs, have been shown to inhibit estrogen sulfotransferase, leading to an apparent estrogenic effect (Kester et al. 2002). A study of the estrogenic potential of several PBDE congeners and hydroxylated metabolites found 11 PBDE congeners and 2 hydroxylated metabolites with estrogenic activity (Meerts et al. 2001). Stoker and co-workers found endocrine effects and developmental delays with exposures to the commercial pentaBDE mixture of 30 and 60 mg/kg/day for 31 days, indicating inhibition of endogenous androgen activity (Stoker et al. 2004). Anti-androgenic and estrogenic activity are of concern as they may lead to a disruption of normal endocrine function and potentially result in reproductive failure and estrogen-related cancers.

REPRODUCTIVE EFFECTS

Male and female rats exposed to the commercial pentaBDE mixture DE-71 exhibited delayed pubertal development with dosing at 30 and 60 mg/kg/day for 5, 21 or 31 days (Stoker et al. 2004). Of the androgen-dependent tissues in exposed male rats, seminal vesicle and ventral prostate weights were reduced, while testes and epididymal weights were not affected. Preputial separation and age of vaginal opening were significantly delayed in exposed female rats. Kuriyama and co-workers evaluated male reproductive health in the rat offspring of dams exposed to BDE-99 in single doses of 60 and 300 µg/kg. Daily sperm production and spermatid counts were significantly decreased (Kuriyama et al. 2005). EPA's Voluntary Children's Chemical Evaluation Program (VCCEP) has concluded that the limited reproductive toxicity data for pentaBDE and octaBDE constitutes an important data need for these chemicals.

CANCER

There is some evidence that decaBDE is carcinogenic in rats and mice from an NTP two-year cancer bioassay (NTP 1986). Statistically significant increases in the incidence of hepatic neoplastic nodules were seen in male rats at 1120 and 2240 mg/kg/day, and in female rats at 2550 mg/kg/day. Increased incidence of hepatocellular adenomas or carcinomas (combined) were seen in male mice at 3200 mg/kg/day; increases relative to controls were seen in male mice dosed at 6650 mg/kg/day and in female mice dosed at 3760 and 7780 mg/kg/day but were not statistically significant. Based on these results, EPA has classified decaBDE as a possible human carcinogen (U.S. EPA 1995). As part of the IRIS assessment of decaBDE, EPA is currently updating its assessment of the carcinogenic potential of decaBDE to reflect the Agency's revised *Guidelines for Carcinogen Risk Assessment* (U.S. EPA 2005). Studies of the carcinogenic potential of pentaBDE and octaBDE have not been conducted.

Pharmacokinetic and Toxicity Profiles of PBDEs in Ecological Receptors

Effects of PBDEs in ecological receptors are currently limited. To date, a variety of endpoints have been assessed in a very limited number of species, primarily invertebrates and fish commonly used in aquatic toxicity testing. Detailed reviews of studies conducted through 1999 can be found in the European Union risk assessments for the PBDEs (ECB 2001; ECB 2002; ECB 2003). No published reports of PBDE toxicity in birds or mammalian wildlife were located. However, recent preliminary reports indicate studies to investigate effects of PBDEs on a variety of sublethal endpoints in avian and mammalian wildlife are underway (SETAC 2004).

PHARMACOKINETICS

In a study of uptake, accumulation and excretion of BDE-47, -99, and -153 by blue mussels, the uptake rate for BDE-47 and BDE-99 was approximately 10 times higher than for BDE-153, but that depuration rates were similar for all three PBDEs (Gustaffson et al. 1999). Uptake efficiencies of BDE-47, BDE-99 and BDE-153 by pike fed trout injected with the congeners were 90%, 62% and 40%, respectively (Burreau et al. 1997). In contrast, uptake of decaBDE is estimated to be quite low (0.02-0.13%) (Kierkegaard

et al. 1999a). Similarly, in carp exposed via the diet for 100 days, BDE-209 did not accumulate (Stapleton et al. 2004a). BDE-47 was distributed in liver, gall bladder, kidneys, brain, chorion of the eye and perivisceral adipose tissue in pike (Burreau and Broman 1998; Burreau et al. 2000).

Recent studies suggest metabolic debromination of higher brominated congeners occurs in fish. Stapleton and co-workers (Stapleton et al. 2004a; Stapleton et al. 2004b) found that BDE-99, -183 and -209 administered via the diet are debrominated in the intestinal tract of the common carp. In a long term feeding study in which 13 tri- through deca-PBDE congeners (purity greater than 96%) were fed to juvenile lake trout, Tomy et al. report the detection of increasing concentrations of lower brominated congeners and occurrence of three penta- and hexa- congeners that were not present in the technical product used to dose the fish, in the food they were fed or in control fish, supporting the hypothesis that higher brominated congeners are debrominated to lower brominated congeners (Tomy et al. 2004).

Hydroxylated and/or methoxylated PBDE congeners have been found in Baltic salmon, herring, ringed seal, and gray seal (Asplund et al. 1997; Asplund et al. 1999; Haglund et al. 1997; Kierkegaard et al. 1999b).

PLANTS

The commercial pentaBDE mixture was essentially non-toxic to a freshwater alga exposed to concentrations ranging from 1.7 ug/L to 26 ug/L in a standard 96-hour toxicity test (ECB 2001). DecaBDE had no effects on the growth of three species of marine algae at concentrations up to 1 microgram per liter (Walsh et al. 1987).

INVERTEBRATES

PentaBDE and octaBDE have been tested for effects on *Daphnia magna*. In 21-day life cycle studies, OctaBDE did not affect survival, reproduction or growth of *Daphnia magna* at concentrations ranging from 0.123 ug/L to 1.96 ug/L (ECB 2003). While some effects were reported for pentaBDE, the significance of the results is confounded by the fact that the test concentrations often exceeded the solubility limits of some of the mixture (ECB 2001). Daphnid reproduction was not affected in this test. PentaBDE did not cause toxic effects to earthworms in a 14-day study (ECB 2001). Chronic exposure of sediment organisms (e.g., *Hyalella azteca*, *Chironomus riparius* and *Lumbriculus variegatus*) to pentaBDE produced no-observable-effect-concentrations (NOECs) in the low milligram per kilogram range for pentaBDE (ECB 2001) and no adverse effects were seen with octaBDE (ECB 2003).

Effects of specific PBDE congeners on two crustacean species have been demonstrated. Full life-cycle studies indicate BDE-47, BDE-99 and BDE-100, at low microgram per liter concentrations affect larval development and population growth rate in the copepod *Nitocra spinipes* (Breitholtz and Wollenberger 2003). BDE-28, BDE-47, BDE-99 and BDE-100 were found to inhibit larval development in the copepod *Acartia tonsa* in the low microgram per liter concentration range (Wollenberger et al. 2005).

FISH

A variety of PBDE mixtures have been found to have very low or no acute toxicity in fish. Commercial mixtures of pentaBDE, octaBDE, and decaBDE had low or no acute toxicity to Japanese medaka and rainbow trout at the solubility limit, even when a carrier solvent was used to increase water solubility (ECB 2001; Hardy 2002).

In an early life stage toxicity study conducted with rainbow trout, no effects were observed on hatching, swim up or larval and fry survival following 21 days waterborne exposure to a pentaBDE mixture. At 60 days post-hatch, statistically significant effects on juvenile fish length and weight were observed at the highest concentration tested (16 µg/L) (ECB 2001). Hornung et al. assessed the toxicity of single congeners, BDE-47, BDE-85, and BDE-99, using an egg injection bioassay developed to assess the toxicity of dioxin-like chemicals in early life stages of rainbow trout. While this bioassay has great sensitivity for detecting dioxin-like toxicity, none of the PBDE congeners tested caused similar early life stage toxicity (Hornung et al. 1996).

As noted above, structural similarities of PBDEs and dioxins led scientists to suspect that PBDEs have toxicological properties similar to dioxins. The potential for PBDEs to possess dioxin-like activity has been explored by measuring induction of the hepatic enzyme cytochrome P450 (CYP1A) because this is a well-established characteristic of chemicals that bind to the AhR, including dioxins. Hepatic CYP1A activity was weakly induced (only 2-3 fold) in rainbow trout larvae injected with a commercial pentaBDE mixture (Norrgrén et al. 1993). Likewise, CYP1A activity was induced in three-spined stickleback fed chironomids contaminated with the same PBDE mixture (Holm et al. 1993). In contrast, in rainbow trout fed food containing BDE-47 and BDE-99, CYP1A activity was inhibited (Tjarnlund et al. 1998). DecaBDE had no effect on CYP1A activity in rainbow trout exposed for 120 days via the diet (Kierkegaard et al. 1999a). Thirteen different PBDE congeners (28, 47, 66, 77, 85, 99, 100, 138, 153, 154, 183, 190, and 209) were administered to juvenile lake trout to assess bioaccumulation and biotransformation (Tomy et al. 2004). In this study, no increase in CYP1A activity was observed at concentrations of the PBDE congeners above those observed in the environment. The finding that commercial PBDE mixtures affected CYP1A activity but that individual congeners did not is consistent with the mammalian literature, and similarly suggests that the enzyme induction is due to some contaminant in the commercial mixtures rather than the PBDE congeners themselves.

A variety of other biochemical endpoints have been assessed in fish exposed to PBDEs. DecaBDE increased liver weight and plasma lactate levels and decreased the number of lymphocytes in rainbow trout dosed with 10 mg decaBDE for up to 120 days via the diet. DecaBDE had no effect on transketolase, ethoxyresorufin-*O*-deethylase, or ethoxycoumarin-*O*-deethylase activity in the same rainbow trout (Kierkegaard et al. 1999a). Fat accumulation in liver and reduced spawning success was observed in three-spined stickleback fed doses of a commercial pentaBDE mixture corresponding to concentrations of 861 and 1630 mg/kg of fat tissue (Holm et al. 1993). Reduced glutathione reductase activity, hematocrit and blood glucose levels were observed in rainbow trout fed a total dose of 21 mg/kg of BDE-47 or 19.5 mg/kg BDE-99 via their

diet over 22 days (Tjarnlund et al. 1998). However, in the same study, no effects on condition factor, liver and spleen somatic indices, white blood cell counts or hemoglobin were observed. Whether these biochemical changes significantly affect health of individual fish or fish populations is currently not established.

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APPENDIX B. Selected International Activities on PBDEs

European Union (EU). The use of both pentaBDE and octaBDE in the EU was banned as of August 2004.

In 2004, the EU reached an agreement with the European chemical industry for the industry to conduct a voluntary program to reduce emissions of decaBDE, and to conduct a program to monitor decaBDE in the environment. In addition, the EU announced it will sponsor a study of developmental neurotoxicity in laboratory animals for decaBDE.

The EU's Restriction on Hazardous Substances (RoHS) directive will prohibit the use of certain chemicals in electrical and electronic equipment as of July 2006. DecaBDE had been on the list of chemicals to be prohibited, but the EU granted an exemption for decaBDE in October 2005.

The EU is also funding the FIRE project (Flame retardants Integrated Risk assessment for Endocrine effects). The objective of the FIRE project is to conduct toxicological studies and exposure assessments to characterize the possible emerging health risk for humans and wildlife of PBDEs, tetrabromobisphenol A and hexabromocyclododecane by endocrine related mechanisms. FIRE is being conducted by a partnership of multiple research centers across Europe; see www.rivm.nl/fire for more information.

International Agreements on Persistent Organic Pollutants (POPs). PentaBDE has been proposed by Norway for listing under two international agreements: the United Nations Economic Commission for Europe (UNECE) Convention on Long-range Transboundary Air Pollution (LRTAP) Protocol on POPs, and the United Nations Environment Program (UNEP) Stockholm Convention on POPs. EPA, with other interested U.S. federal agencies, is actively involved in the consideration of the proposals in accordance with the treaties' respective review processes and the participatory status of the U.S. under these agreements. For more information on the LRTAP POPs protocol and the proposal by Norway, see <http://www.unece.org/env/lrtap/welcome.html>, <http://www.unece.org/env/popsxg/proposals%20for%20NEW%20pops.htm>, and the Report of the 23rd Session of the Executive Body at <http://www.unece.org/env/eb/welcome.23.html>. For information on the Stockholm Convention and Norway's proposal, see <http://www.pops.int/default.htm>, http://www.pops.int/documents/meetings/cop_1/chemlisting/Default.htm, and the Report of the First meeting of the Persistent Organic Pollutants Review Committee at http://www.pops.int/documents/meetings/poprc/meeting_docs/reports/default.htm.

Organization for Economic Cooperation and Development (OECD). The Brominated Flame Retardant (BFR) Clearinghouse of the OECD has developed hazard/risk information fact sheets on the PBDEs, as well as HBCD and TBBPA, and has identified critical data gaps. OECD intends to follow the development of new information on BFRs, update the fact sheets every 2-3 years, and work to improve cooperation between producers and users of BFRs in order to reduce emissions to the environment.

Arctic Council. The Arctic Council is an inter-governmental forum addressing Arctic issues whose members include Canada, Denmark, Finland, Iceland, Norway, Sweden, the Russian Federation and the United States. The objectives of the Council's Brominated Flame Retardants Project are to: reduce or eliminate sources and releases of BFRs that are found in the Arctic environment; identify and develop safe waste-handling and recycling practices for products containing brominated flame retardants; and identify alternative flame retardant chemicals and technologies and promote safe alternatives.

APPENDIX C. PBDE Research and Assessment Activities Conducted by or Funded by EPA

Levels in the Environment and Biota

Breast Milk Measurements in California

Under a grant from EPA, the California Environmental Protection Agency is collecting breast milk samples and analyzing them for the presence of PBDEs.

Analysis of PBDEs in Breast Milk and House Dust

EPA plans to issue a cooperative agreement to measure PBDEs and hexabromocyclododecane (HBCD) in breast milk; assess whether levels in dust correlate with body burdens of PBDEs and HBCD; explore whether body burdens of PBDEs are decreased in the subjects via lactation; and explore possible biological differences among women that might explain variability in body burdens.

Pilot Study on Concentrations of PBDEs in Human Milk

EPA has funded a study by Pennsylvania State University and the Centers for Disease Control and Prevention (CDC) to measure concentrations of PBDEs in human milk breast milk in two very different populations of 20 women each: Amish women, and non-Amish woman living in more traditional suburban settings in Pennsylvania. The purpose of the study is to assess whether lifestyle factors, demographics, or other determinants of exposures appear to be correlated with levels of these chemicals.

Methods Advancement in Milk Analysis

As part of the Methods Advancement in Milk Analysis (MAMA) study, in support of the National Children's Study, scientists in EPA's National Health and Environmental Effects Research Laboratory (NHEERL) are working in collaboration with the CDC to measure and identify PBDEs present in the milk and serum of women in North Carolina. The research will assess diet, lifestyle, occupation, stage of lactation, sample collection and storage methods as significant variables.

PDBEs in Lake Superior Watershed

EPA has funded a study by the Minnesota Pollution Control Agency (MPCA) to assess the prevalence, potential for local sources and accumulation trends of PBDEs in the St. Louis River and western Lake Superior watershed. This project will estimate the prevalence of PBDEs in surficial sediments and fish. Trends in PBDE accumulation in ambient and industrially-impacted locations will be examined by analyzing sediment cores from a remote lake and the Duluth-Superior Harbor.

Levels of PBDEs in Eggs of Wisconsin Cormorants

EPA has funded a Wisconsin Department of Natural Resources project to investigate the presence and levels of PBDEs in double crested cormorant eggs taken from Lake Michigan and the Bay of Green Bay. Cormorant eggs to be analyzed for PBDEs include

archived eggs collected by the U.S. Fish and Wildlife Service during the 1970s, 1980s and 1990s (between 25 and 40 eggs).

PBDEs in Cord Blood, Great Lakes Sediments and Fish

Under an EPA STAR (Science to Achieve Results) grant to Indiana University, researchers will measure PBDE concentrations in umbilical cord blood from 50 newborn U.S. infants and samples of their mothers' blood collected at delivery to assess fetal exposure to PBDEs. The researchers will also measure PBDEs in Great Lakes sediment cores and fish to assess long term trends of PBDEs in environment.

PBDEs at the Calumet Water Reclamation Plant (Chicago)

This project will characterize levels of 14 PBDE congeners in aqueous and sludge samples at various stages in the treatment facility, including the influent, effluent, digestion sludge, and final sludge product. The project is a screening level analysis of the fate (including transformations and degradations) of PBDEs within the water reclamation plant. This is a collaborative effort among U.S. EPA, the U.S. Department of Agriculture (USDA), the U.S. Geological Survey, and the Metropolitan Water Reclamation District of Greater Chicago. Samples will be collected in 2005 and early 2006, with a final report expected in the summer of 2006.

POTW Measurements of PBDEs

A scientist in EPA Region 10 measured levels of PBDEs in samples of effluents and biosolids collected from five publicly-owned treatment works (POTWs) in the state of Washington in 2002.

End-of-Life/Disposal

Leaching of Hazardous Chemicals from Discarded Electronic Devices

EPA has provided funding to the University of Florida to evaluate potential environmental impact of flame retardants in plastics in electronic devices, including potential for leaching of flame retardants from the plastics.

Debromination and Biotransformation of PBDEs in sediments

Under an EPA STAR grant to Purdue University, researchers will assess whether decaBDE undergoes reductive debromination and, if so, will quantify the products of this biotransformation.

Combustion-derived PBDEs and PBDD/Fs: Electronics recycling and municipal waste

EPA's National Risk Management Laboratory has been studying the incineration of materials that may contain PBDEs. Researchers have measured brominated organic compounds in municipal waste combustor flue gas; examined incineration of recycled phone boards, motherboards and keyboards; and taken samples from a municipal waste combustor and to analyze for presence of brominated organic compounds. They are now developing methods to measure PBDEs and brominated dioxins and furans in combustor emission samples.

PBDEs Toxicology and Health Risk Assessment

Data for Calculating a pentaBDE Margin of Exposure

EPA has issued a contract to analyze levels of PBDEs in blood samples from pregnant rats, fetuses and offspring exposed to the commercial pentaBDE mixture, DE-71. These data will allow comparison of blood or adipose tissue concentrations in humans to those found in rats for what appear to be the critical endpoints in rodent studies. This information should allow for a screening level analysis of the margin-of-exposure for this class of chemicals.

Neurological Consequences of PBDE-Induced Decreases in Thyroid Hormones During Development

EPA's NHEERL is conducting animal studies of the relationship between thyroid hormone decreases caused by PBDEs during development and alterations in neurobehavioral outcomes. Research is currently focused on the commercial pentaBDE mixture, DE-71.

Low Dose Effects of Thyroid Toxicants on Neurodevelopment

Under an EPA STAR grant, researchers at the University of Massachusetts are examining the effects of several thyroid toxicants, including PBDEs, on neurodevelopmental endpoints in rats. The study will characterize dose-response relationships between PBDE levels, thyroid hormone levels, and neurodevelopmental endpoints.

Studies of Potential Endocrine Disruption by pentaBDE

Researchers in EPA's NHEERL used the commercial pentaBDE product and individual PBDE congeners contained in that mixture to test the sensitivity of different test rat study protocols for identifying thyroid active chemicals, and to identify potential endocrine disrupting effects. This work has been published by T.E. Stoker and colleagues in *Toxicological Sciences* (2004) and *Toxicology and Applied Pharmacology* (2005).

Toxicity and Estrogenic Activity of Polybrominated Diphenyl Ethers (PBDEs)

Under a grant from EPA, the Wisconsin Department of Natural Resources is conducting research to: 1) determine estrogenic activity of BDE-47 and BDE-99 using the E-screen assay; 2) determine the acute and chronic toxicity of BDE-47 to the aquatic invertebrate, *Ceriodaphnia dubia*; 3) determine the concentration of PBDEs in sediments of the Sheboygan River basin; and 4) determine the concentration of PBDEs in wastewater treatment plant and industrial effluents in the Sheboygan River basin.

PBDEs/PCBs and Thyroid Outcomes

An EPA STAR grant is funding research by the Wisconsin Department of Health to characterize exposure to PBDEs from consumption of Lake Michigan sport fish and to determine mechanisms by which PBDEs in Great Lakes fish may act separately or synergistically with PCB exposure to impair thyroid function.

Pharmacokinetics of PBDEs in Mice

Scientists in EPA's NHEERL are investigating the absorption, distribution, metabolism, and excretion of the tetraBDE congener BDE-47 in adult mice and during development. A physiologically based pharmacokinetic model is being developed to predict the behavior under multiple scenarios. The tissue distribution, metabolism, and elimination of pentaBDE congeners BDE-99 and -100, and hexaBDE congener BDE-153 are also being investigated in mice. Articles reporting on this work by D.F. Staskal and colleagues have been published in *Toxicological Sciences* (2005).

Fetal Exposure Modeling

An EPA STAR grant to Research Triangle Institute is supporting work to develop a physiologically-based pharmacokinetic (PBPK) model for BDE-47 and BDE-99 in an animal model system (rats) that can be used to estimate fetal exposures to PBDEs in humans. Necessary partitioning and metabolic parameters will be measured using *in-vivo* and *in-vitro* experiments. The developed PBPK model will be useful for studying different aspects of exposure, including the impact of chronic and intermittent exposures on time-sensitive, developmental events. The exposures of a group of mothers and their newborn children to the target congeners will be determined.

Mode of Action for Developmental Neurotoxicity of PBDEs

Scientists in EPA's NHEERL are conducting research to evaluate intracellular signaling as a potential mode of action for the developmental neurotoxicity of PBDEs. Both *in vitro* and *in vivo* approaches will be utilized to address this issue in PBDE mixtures and selected individual congeners. The *in vitro* effects will be compared with *in vivo* studies in terms of the effects and the concentrations at which effects are observed. In addition, the results from PBDE mixtures and individual congeners will be compared with other structurally related chemicals. This research will aid in understanding a common mode of developmental neurotoxicity for these persistent chemicals.

Developmental Neurotoxicity of Commercial pentaBDE and BDE-47 in Mice

Scientists in EPA's NHEERL are conducting research to repeat the studies of Eriksson and co-workers that have found developmental neurotoxic effects of PBDEs in mice. These studies will also conduct long-term dosing of the dam as well as the pup and the body burdens will be determined both experimentally and by pharmacokinetic modeling approaches.

Bioavailability of PBDEs from House Dust

Scientists in EPA's NHEERL are collaborating with scientists at USDA and Duke University to investigate the bioavailability of PBDEs from dust in rats. Standardized samples of house dust will be used and over 20 PBDE congeners measured.

VCCEP

Chemicals of potential concern to children's health are the subject of evaluation in the pilot Voluntary Children's Chemical Evaluation Program (VCCEP). VCCEP was developed to ensure that there are adequate publicly available data to assess the impact that industrial chemicals may have on children. PentaBDE, octaBDE and decaBDE are

among the chemicals being assessed in the VCCEP pilot. Further information regarding VCCEP is available at <http://www.epa.gov/chemrtk/vccep>.

IRIS Assessments for PBDEs

EPA is conducting reviews of the available toxicology data for tetra-, penta-, hexa- and decaBDE congeners under its Integrated Risk Information System (IRIS) program. Completion of these assessments is projected for 2006.

Alternatives Analysis

Furniture Flame Retardancy Partnership

The Furniture Flame Retardancy Partnership is a joint venture of the furniture industry, chemical manufacturers, environmental groups and EPA to better understand fire safety options for the furniture industry. Through the Furniture Flame Retardancy Partnership, EPA and its partners hope to identify and move toward environmentally friendly approaches to meeting fire safety standards. The partnership initially focused on providing up-to-date toxicological and environmental information on flame retardants used in furniture foam, as alternatives to pentaBDE, so that furniture manufacturers and suppliers are able to make informed decisions about which chemicals to use. The Partnership also plans to develop a process for identifying and developing data needed to assess potential risks from flame retardant chemicals used in furniture. More information is available at <http://www.epa.gov/opptintr/dfe/pubs/projects/flameret/index.htm>.

Market Analysis of PBDEs

In 2003, an EPA contractor prepared a review of market data on PBDEs. The report included a review of PBDEs suppliers, usage data, and a review of information available at that time on alternatives to pentaBDE in flexible polyurethane foam.

Regulatory Activities

SNUR for pentaBDE and octaBDE

EPA has proposed a Significant New Use Rule (SNUR) under section 5(a)(2) of the Toxic Substances Control Act (TSCA) that would require manufacturers and importers to notify EPA at least 90 days before commencing the manufacture or import of pentaBDE or octaBDE. The required notice would provide EPA with the opportunity to evaluate each chemical substance's use, and if necessary, to prohibit or limit such activity before it occurs. EPA expects to finalize the SNUR in 2006.

Residential Furniture SNUR

EPA is preparing to propose a SNUR under section 5(a)(2) of TSCA for flame retardants identified as candidates for use to meet the residential upholstered furniture (RUF) flammability standards under consideration by the State of California and the U.S. Consumer Product Safety Commission (CPSC). Sixteen chemical substances/categories,

including decaBDE, are being considered for inclusion in the SNUR. The SNUR would require persons who intend to manufacture, import, or process any of these chemical substances, or articles containing them, for use as a flame retardant (FR) in RUF to notify EPA at least 90 days before commencing such activity. The required notice would provide EPA with the opportunity to evaluate each chemical substance's use as a FR in RUF, and if necessary, to prohibit or limit such activity before it occurs.

Monitoring of Drinking Water

EPA proposed its Unregulated Contaminant Monitoring Regulation (UCMR 2) under the Safe Drinking Water Act in the Federal Register on August 22, 2005 (70 FR 49093). Under UCMR 2, EPA is proposing to require 3,910 public water systems to monitor for 26 unregulated chemicals, including BDE congeners 47, 99, 100 and 153. EPA expects to publish the final regulation in 2006 and monitoring is expected to occur during the 2007 to 2010 timeframe. The data collected through the UCMR program will be used to assess the level of these chemicals in finished drinking water and assist the Agency in deciding whether a drinking water regulation is needed.

APPENDIX D. PBDEs Research and Assessment Activities at Other U.S. Federal Agencies

Centers for Disease Control and Prevention (CDC). As part of the National Health and Nutrition Examination Survey (NHANES), CDC is analyzing blood samples collected in 2003-2004 for levels of 10 PBDE congeners. Results of this nationally-representative statistical sample are expected in 2006, for two age groups (ages 12- 19 years, and age 20 and older) as well as gender and race/ethnicity sub-groups. The survey is continuous, and additional results will be available in future years to allow evaluation of any trends. CDC is also conducting several additional studies of PBDEs aimed at determining body burdens in segments of the population that may be more highly exposed and identifying which routes of exposure are of main importance for the human population.

Food and Drug Administration (FDA). FDA has been working with the food and feed industries to understand sources of PBDEs and other persistent contaminants. FDA is conducting studies on methods for the analysis of PBDEs in different food and feed matrices, and has measured PBDEs in select fish samples. In 2006, FDA will include appropriate food and feed in a sampling program to assess PBDE levels, and will use this information to assess dietary PBDE exposures to determine appropriate risk management options.

National Institute of Standards and Technology (NIST). NIST is conducting research to examine the rates by which PBDEs are emitted from plastics over time due to natural weathering, increased temperatures and irradiant exposures. NIST is also conducting studies to measure PBDEs in house dust, California sea lions, and rainbow trout.

National Oceanic and Atmospheric Administration (NOAA). NOAA has measured levels of PBDEs in mussel tissue and sediments near the World Trade Center site, and in sediments in the Chesapeake Bay.

National Toxicology Program (NTP). NTP is currently conducting a subchronic toxicity study of commercial pentaBDE (DE-71) in rats and mice. NTP is also planning to do a chronic study to look for cancer potential, but plans for this study will not be finalized until after the subchronic study is completed. In addition, NTP is conducting studies of gene expression and tissue distribution for BDE congeners 47, 99, and 153.

U.S. Department of Agriculture (USDA). USDA is conducting research on the absorption, disposition, metabolism, and excretion (ADME) of PBDEs. Studies of ADME in rats have been conducted on commercial pentaBDE, octaBDE and decaBDE mixtures. Rodent ADME studies have also been conducted on BDE congeners 47, 99, 100, 154 and 209. Studies in rats are planned for BDEs 153 and 183, along with further study of BDE-209. ADME studies of the pentaBDE mixture and BDE-47 are also being conducted in chickens. USDA has also conducted some measurements of PBDE levels in meats and poultry, and will be extending these analyses to additional food samples.

U.S. Geological Survey (USGS). The USGS is conducting studies to: measure indoor air levels of PBDEs in homes and offices; measure levels of PBDEs in fish and fish-eating birds; evaluate the environmental fate of PBDEs; and determine the potential for weathered recycled computer equipment to contaminate nearby soil and sediments.