United States Environmental Protection Agency

Design for the Environment U.S. EPA

FLAME RETARDANT ALTERNATIVES FOR HEXABROMOCYCLODODECANE (HBCD)

FINAL REPORT

June 2014

EPA Publication 740R14001

Executive Summary

This report provides information on hexabromocyclododecane (HBCD; CASRN 25637-99-4; 3194-55-6) used as a flame retardant in polystyrene building insulation, possible substitutes, and alternative materials. The report was developed by the U.S. Environmental Protection Agency (EPA) with input from a partnership of stakeholders from business, government, academia, and environmental organizations. According to technical experts on the Partnership, between 2011 and 2014 there were only three viable flame retardant alternatives to HBCD for use in expanded and extruded polystyrene foam (EPS and XPS) insulation under current manufacturing processes. Alternative materials are also available as substitutes to HBCD-containing insulation. These alternatives may require additive flame retardants or other treatment to meet fire safety requirements. This report:

1) Identifies viable and non-viable flame retardant alternatives for HBCD in polystyrene building insulation foam;
2) Describes uses and provides an overview of end-of-life scenarios and exposure to HBCD;
3) Provides hazard profiles for HBCD and the three chemical alternatives; and
4) Provides an overview of relevant alternative materials.

Based on DfE AA criteria and guidance, the hazard profile of the butadiene styrene brominated copolymer (CASRN 1195978-93-8) shows that this chemical is anticipated to be safer than HBCD for multiple endpoints. Due to its large size, lack of low molecular weight (MW) components, and un-reactive functional groups, human health and ecotoxicity hazard for this polymer are measured or predicted to be low, although experimental data were not available for all endpoints. In general the exposure potential to the butadiene styrene brominated copolymer is expected to be lower than the other chemicals in this assessment because it is a large polymer and is unlikely to be released from the polystyrene. However, this alternative is inherently persistent and its long-term behavior in the environment is not currently known. Chemical suppliers have commercialized this polymer, and polystyrene manufacturers are testing it in their products to ensure that the polystyrene will meet all performance standards. The hazard designations for this alternative are based upon high MW formulations of the polymer, where all components have a MW >1,000. The polymer is regulated with a Significant New Use Rule that was finalized in June 2013. Manufacture (or import) of the polymer requires notification to EPA except in these cases: (1) the MW of the polymer is in the range of 1,000 to 10,000 daltons, or (2) the MW of the polymer is ≥10,000 daltons and less than 5 percent of the particles are in the respirable range of 10 microns or less (U.S. EPA 2013).

The hazard profiles of the tetrabromobisphenol A (TBBPA)-bis brominated ether derivative (CASRN 97416-84-7) and TBBPA bis(2,3-dibromopropyl) ether (CASRN 21850-44-2) show that these chemicals have limited data sets for human health endpoints and hazard designations show a potential for toxicity. These two chemicals are also anticipated to have High potential for bioaccumulation.

Background

In August 2010, EPA released the HBCD Action Plan. The Action Plan summarized hazard, exposure, and use information regarding environmental and health risks associated with HBCD.

HBCD is a flame retardant that has been found to have persistent, bioaccumulative, and toxic (PBT) characteristics. HBCD use as a flame retardant in EPS and XPS accounts for more than 95% of HBCD applications. EPS and XPS are used as rigid foam insulation in the building and construction industry. A small volume of HBCD is used in textiles and high-impact polystyrene (HIPS).

As part of the Agency's efforts to manage chemical risks, the Action Plan called upon the Design for the Environment (DfE) Program to conduct an alternatives assessment for HBCD. A DfE Alternatives Assessment identifies and compares potential alternatives that can be used as substitutes to replace chemicals that the Agency has designated for action. DfE alternatives assessments provide information on functional class, intrinsic hazard, exposure properties, and environmental fate for chemical alternatives. The information in DfE alternatives assessments can influence the selection of safer, more sustainable alternatives when combined with other information that is not the focus of DfE Alternatives Assessments, such as performance and cost.

Goal of the Partnership and Report

DfE convened a multi-stakeholder partnership to assess the potential human health and environmental hazards of HBCD and its alternatives for use in EPS and XPS foam. The information presented in this report is based on the Partnership's knowledge and the DfE Program's research. Chapter 1 of the report provides background information on HBCD and defines the report's purpose and scope. Chapter 2 discusses the uses, end-of-life scenarios, and exposure potential of HBCD. Chapter 3 offers background information on flame retardants and outlines which flame retardants are and are not included in the alternatives assessment. Chapter 4 explains the hazard evaluation methodology and includes the hazard profiles for HBCD and the three identified alternatives. Chapter 5 summarizes the results of the assessment, discusses considerations for selecting flame retardants and includes an overview of alternative materials. Since the primary use for HBCD is in EPS and XPS foam insulation, the project scope does not include alternatives to HBCD for its minor uses in textiles and HIPS. Alternatives to HBCD for these uses are included in a separate DfE Alternatives Assessment for decabromodiphenyl ether (decaBDE). Flame retardant performance and costs of HBCD and the three alternatives were not assessed in-depth in this report.

Results

Members of the Partnership identified many chemicals as potential alternatives; however, only three chemicals were identified as viable alternatives to HBCD in EPS and XPS foam: a butadiene styrene brominated copolymer (CASRN 1195978-93-8), a TBBPA-bis brominated ether derivative (CASRN 97416-84-7), and TBBPA bis(2,3-dibromopropyl) ether (CASRN 21850-44-2). Only three alternatives were identified for evaluation in this report because flame retardants for EPS and XPS foam must allow the material to comply with fire safety codes while not compromising the performance of the foam. All three alternatives are brominated. No non-brominated flame retardants are known to be compatible in polystyrene manufacturing and associated flame tests. Figure ES-1 summarizes the hazard information for HBCD and the three alternatives assessed. Few measured experimental data were available for the TBBPA-bis brominated ether derivative; therefore, estimated hazard designations were determined using TBBPA bis(2,3-dibromopropyl ether) (CASRN 21850-44-2) as an analog.

The human health endpoints evaluated in DfE alternatives assessments include acute toxicity, carcinogenicity, genotoxicity, reproductive toxicity, developmental toxicity, neurotoxicity, repeated dose toxicity, skin sensitization, respiratory sensitization, eye irritation, and dermal irritation. HBCD has been assigned a High hazard designation for developmental neurotoxicity, a Moderate hazard designation for reproductive toxicity and repeated dose toxicity, and an estimated Moderate hazard designation for carcinogenicity and neurotoxicity; other health endpoints have Low or Very Low hazard designations. The butadiene styrene brominated copolymer has Low hazard designations (either measured or estimated) for most human health endpoints due to its high MW and limited potential for absorption; there is one Moderate hazard designation for the eye irritation endpoint based on experimental data. The TBBPA-bis brominated ether derivative and TBBPA bis(2,3-dibromopropyl) ether have a Moderate hazard designation for carcinogenicity, mutagenicity, reproductive toxicity, developmental toxicity, and repeated dose toxicity based on potential alkylating properties. Low hazard designations have been assigned to these similar substances for acute toxicity, neurotoxicity, skin sensitization and irritation.

The ecotoxicity endpoints evaluated in DfE alternatives assessments include acute and chronic aquatic toxicities. HBCD is aquatically toxic and has Very High hazard designations for both acute and chronic aquatic toxicity. Aquatic toxicity for the three alternatives is Low, driven by their lack of appreciable water solubility leading to "no effects at saturation" (NES). Ecotoxicity data for terrestrial species was limited, and thus the potential for impacts on high trophic level and terrestrial wildlife from HBCD and its alternatives or associated degradation products is unclear.

The environmental fate of HBCD and the three alternatives is described primarily in terms of persistence and bioaccumulation potential. All three chemicals have High or Very High persistence designations, a quality typical for the majority of flame retardants. Long-term fate of the three alternatives in the environment is not well understood. The butadiene styrene brominated copolymer is estimated to have Low bioaccumulation potential due to its size (average MW >1,000 daltons) and lack of low MW components, while HBCD, the TBBPA-bis brominated derivative, and TBBPA bis(2,3-dibromopropyl) ether have Very High, High, and High potential for bioaccumulation.

Under conditions where fire or incineration occurs, a halogenated substance may: contribute to halogenated dibenzodioxin and dibenzofuran formation, increase the generation of PAHs, and impact fire parameters such as smoke and carbon monoxide (Sidhu, Morgan et al. 2013). However, combustion reactions are complex and variable and make inclusion of combustion by-products in hazard assessment challenging. Both halogenated and non-halogenated flame retardants may yield other toxic by-products that would need to be compared, not only halogenated dioxins and furans. For these reasons, the pyrolysis transformation products are not assessed in this report.

In addition to the chemical hazard assessment of HBCD and its alternatives, Chapter 5 of the report includes general information about alternative insulation materials. These technologies include rigid board alternatives (e.g., similar to EPS and XPS), alternatives for certain functional uses (e.g., blanket insulation, foamed-in-place insulation), and specialty and emerging alternative

materials (e.g., aerogel, carbon foam). The report does not assess these materials, does not compare them to EPS or XPS, and does not assess flame retardancy needs for each of these materials.

How to Use This Report

The intended audience for the report includes, but is not limited to, chemical manufacturers, product manufacturers, retailers, consumers, non-governmental organizations (NGOs), consultants, and state and federal regulators. Three possible uses of this report include: identification of potential substitutes; selection of alternative chemicals based on comparative hazard assessment; and use of hazard information for further analysis and decision-making.

This report allows stakeholders interested in chemical substitution to identify functional substitutes for HBCD in EPS and XPS foam. The list of potential alternatives introduced in Chapter 3 includes chemicals identified by stakeholders as viable, functional alternatives, as well as chemicals that are not considered functional alternatives. Decision-makers can understand and compare the hazard concerns associated with the four chemicals using the profiles in Chapter 4. The inclusion of a chemical in this assessment does not indicate environmental- or health-based preferability. Manufacturers considering the potential functional alternatives in this report will likely also conduct performance testing to confirm an alternative's performance in their product. Although outside of the report scope, decision makers should also consider the human health and environmental impacts of insulation's non-flame retardant additives (e.g., synergists and stabilizers) discussed in Chapter 2 of the report.

Chapter 4 describes the hazard criteria, data interpretation, and information used to assign hazard values in each category. The chapter provides a human health and environmental profile for each chemical that is based on empirical data, and enhanced with modeling and expert judgment to fill data gaps. Where toxicity is estimated in the absence of measured data, DfE encourages users to be conservative in the interpretation of the hazard profiles. Chemicals used at high volumes, or likely to be in the future, should be of high priority for further empirical testing.

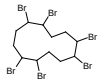
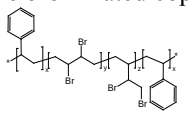
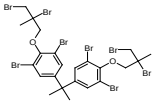
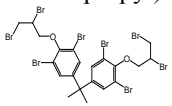
The information in this report can be used to inform or supplement further analyses such as risk assessments or life-cycle assessments (LCAs) on preferred alternative chemicals. The criteria used to develop the hazard assessments in this report can also be used to inform green chemistry design, if availability of safer alternatives is limited.

ES-1 Hazard Summary for HBCD and Alternatives

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.

This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

d This hazard designation would be assigned MODERATE for a potential for lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations.
§ Based on analogy to experimental data for a structurally similar compound.
¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical For full chemical name and relevant trade names see the hazard profiles in Section 4.8	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization[1]	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Hexabromocyclododecane (HBCD) 	25637-99-4; 3194-55-6	L	*M*	L	M	H	*M*	M	L		VL	VL	VH	VH	H	VH
Butadiene styrene brominated copolymer¥ 	1195978-93-8	L	*L*	L	L	L	*L*	L[d]	L		M	L	*L*	*L*	*VH*	*L*
TBBPA-bis brominated ether derivative¥ 	97416-84-7	*L*[§]	*M*[§]	*M*[§]	*M*[§]	*M*[§]	*L*	*M*[§]	*L*[§]		*L*	*L*	*L*	*L*	*H*	*H*
TBBPA bis(2,3-dibromopropyl) ether¥ 	21850-44-2	L	*M*	M	*M*	*M*	*L*	*M*	L		L	L	L	*L*	VH	*H*

[1] At this time, there are no standard test methods for respiratory sensitization and no test data; as a result there was no designation for this endpoint.

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List of Acronyms and Abbreviations

ACR	Acute to chronic ratio
AIM	Analog Identification Methodology
ASTM	American Society for Testing and Materials
ATSDR	Agency for Toxic Substances and Disease Registry
BAF	Bioaccumulation Factor
BEARHFTI	California Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation
BCF	Bioconcentration Factor
C&D	Construction and demolition
CDR	Chemical Data Reporting
CFC	Chlorofluorocarbon
ChV	Chronic value
CPSC	Consumer Product Safety Commission
DecaBDE	Decabromodiphenyl ether
DfE	Design for the Environment
EC_{50}	Half maximal effective concentration
ECOSAR	Ecological Structure Activity Relationships
EDSP	Endocrine Disruptor Screening Program
E_h	Redox potential
EIFS	Exterior Insulating and Finishing System
EPA	U.S. Environmental Protection Agency
EPI	Estimation Programs Interface
EPS	Expanded polystyrene foam
FPQA	Food Quality Protection Act
FPSF	Frost Protected Shallow Foundation
FM	Factory Mutual
GHS	Globally Harmonized System of Classification and Labeling of Chemicals
HBr	Hydrogen bromide
HFC	Hydrofluorocarbon
HIPS	High-impact polystyrene
HPV	High production volume
HSDB	Hazardous Substances Data Bank
IARC	International Agency for Research on Cancer
IBC	International Building Code
ICF	Insulating Concrete Form
IRC	International Residential Code
IRIS	Integrated Risk Information System
IUR	Inventory Update Reporting
K_{oa}	Octanol/air partition coefficient
K_{oc}	Soil adsorption coefficient
K_{ow}	Octanol/water partition coefficient
LC_{50}	Median lethal concentration
LCA	Life-cycle assessment
LD_{50}	Median lethal dose

LFL	Lower limit of flammability
LOAEL	Lowest observed adverse effect level
LOEC	Lowest observed effect concentration
LRTAP	Long-Range Transboundary Air Pollution
MDI	Methylene diphenyl diisocyanate
MF	Molecular formula
MITI	Ministry of International Trade and Industry
MSDS	Material Safety Data Sheet
MW	Molecular weight
NES	No Effects at Saturation
NFPA	National Fire Protection Association
NGO	Non-governmental organization
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIST	National Institute of Standards and Technology
NOAEL	No observed adverse effect level
NOEC	No observed effect concentration
NTP	National Toxicology Program
OECD	Organisation for Economic Co-operation Development
P2	Pollution Prevention
PBDE	Polybrominated diphenyl ether
PBT	Persistent, bioaccumulative, and toxic
PET	Polyethylene terephthalate
pMDI	Polymeric methylene diphenyl diisocyanate
POP	Persistent organic pollutant
POPRC	Persistent Organic Pollutants Review Committee
QSAR	Quantitative Structure Activity Relationships
RDP	Resorcinol-bis-diphenyl phosphate
REACH	**R**egistration, **E**valuation, **A**uthorisation and Restriction of **Ch**emical Substances
SAR	Structure Activity Relationship
SIAP	Screening Information Dataset Initial Assessment Profile
SF	Sustainable Futures
SIP	Structural Insulated Panel
SNUR	Significant New Use Rule
SPF	Spray polyurethane foam
TBBPA	Tetrabromobisphenol A
TCPP	Tris(chlorpropyl) phosphate
TDI	Toluene diisocyanate
TSCA	Toxic Substances Control Act
UBC	Uniform Building Code
UFL	Upper limit of flammability
UL	Underwriters Laboratories
UNECE	United Nations Economic Commission for Europe
XPS	Extruded polystyrene foam

1 Introduction

1.1 Background

As part of its effort to enhance the safety of chemicals, the U.S. Environmental Protection Agency (EPA) has taken steps to identify chemicals that may pose environmental and health concerns. Between 2009 and 2011, EPA developed action plans that considered both potential regulatory and voluntary actions. In August 2010, EPA released the Hexabromocyclododecane (HBCD) Action Plan[1]. This Action Plan summarized hazard, exposure, and use information to help evaluate the environmental and health risks associated with HBCD[2].

HBCD is a brominated flame retardant found worldwide in the environment and wildlife. Human exposure is evidenced from its presence in breast milk, adipose tissue, and blood. It bioaccumulates and biomagnifies in the food chain. It persists and is transported long distances in the environment, and is highly toxic to aquatic organisms. HBCD also presents potential human health concerns based on animal test results indicating potential reproductive, developmental, and neurological effects.

HBCD is a flame retardant most commonly used in expanded polystyrene foam (EPS) and extruded polystyrene foam (XPS). EPS and XPS are used as insulation in the building and construction industry. HBCD is also used in materials such as textile back coatings on institutional carpet tiles or upholstery and some military fabrics (U.S. EPA 2012). A minor use of HBCD is in high-impact polystyrene (HIPS) for electrical and electronic applications such as audio-visual equipment, refrigerator linings, and in wire and cable (U.S. EPA 2010).

The Action Plan stated EPA's intent to conduct this Design for the Environment (DfE) Program alternatives assessment: *Flame Retardant Alternatives for Hexabromocyclododecane (HBCD).* DfE's Alternatives Assessment Program helps industries choose safer chemicals and provides a basis for informed decision-making by developing an in-depth comparison of potential human health and environmental impacts of chemical alternatives. DfE convened a multi-stakeholder partnership to help select and evaluate flame retardant alternatives to HBCD and develop this report. Partnership representatives from industrial, academic, governmental, and non-governmental organizations (NGOs) engaged with DfE to provide input from a variety of different viewpoints. The chemical alternatives chosen for this report were included because they were identified by stakeholders as potential functional alternatives. Including these alternatives does not indicate that EPA considers them to be preferable in terms of environmental or health hazard, or any other metric. This report did not evaluate efficacy of these alternatives which may be related to specific material and product applications and related standards. Stakeholders provided professional judgment about whether chemicals are likely to meet flammability tests in

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[1] The Hexabromocyclododecane (HBCD) Action Plan is available online at: http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/hbcd.html.

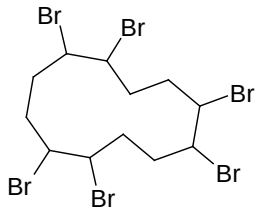
[2] HBCD should not be confused with hexachloro-1,3-butadiene (HCBD). For information about HCBD, see http://www.epa.gov/opptintr/chemtest/pubs/hexchbut.html.

EPS and XPS. The report does provide information that will enable more informed selection of alternative flame retardants to HBCD for EPS and XPS.

Several international governmental entities have begun to take actions towards regulating HBCD in recent years, including the United Nations Economic Commission for Europe (UNECE) Convention on Long-Range Transboundary Air Pollution (LRTAP) (United Nations Economic Commission for Europe 2011), the Stockholm Convention on Persistent Organic Pollutants (POPs) (Stockholm Convention on Persistent Organic Pollutants 2008), the European Union (European Chemicals Agency 2011), Canada (Environment Canada 2010), and Australia (Australian Department of Health and Aging: National Industrial Chemicals Notification and Assessment 2008). In the United States, the HBCD Action Plan proposed several regulatory actions to manage the risk that may be presented by HBCD (U.S. EPA 2010). As the regulation of HBCD is considered in the U.S. and internationally, this alternatives assessment will be an important resource both in reporting on the environmental and human health profiles of HBCD alternatives and in helping product manufacturers select safer alternative flame retardants. The information will help reduce the potential for the unintended consequences that could result if functional but poorly understood or more hazardous alternatives are chosen as chemical substitutes to HBCD.

HBCD is a category of brominated flame retardants, consisting of 16 possible isomers. It has a molecular formula (MF) of $C_{12}H_{18}Br_6$ and its structure consists of a ring of 12 carbon atoms to which 18 hydrogen and six bromine atoms are bound. HBCD may be designated as a non-specific mixture of all isomers (Hexabromocyclododecane; CASRN: 25637-99-4) or as a mixture of three main diastereomers (1,2,5,6,9,10-hexabromocyclododecane; CASRN: 3194-55-6). Both mixtures are listed on the Toxic Substances Control Act (TSCA) Inventory and have substantial use in U.S. commerce (10-50 million pounds in 2005). A representative structure of HBCD is shown in Figure 1-1 below.

Figure 1-1. Representative Structure of HBCD



HBCD is an effective flame retardant for building insulation materials and does not compromise the physical properties of the foam. HBCD is uniquely suited for use in EPS and XPS foam due to its effectiveness at low concentration levels, compatibility with current manufacturing processes and chemicals, and low water solubility. Alternatives to HBCD must meet the same functional requirements; there are currently few viable[3] alternatives to HBCD for EPS or XPS.

[3] Viability refers to the functional performance of a chemical as a flame retardant in EPS and XPS foam, not the environmental preferability of the chemical nor other product performance criteria.

Alternatives to HBCD have been discussed previously in reports published by the European Commission and the University of Massachusetts at Lowell (Morose 2006; IOM Consulting 2009). These assessments looked at alternatives to HBCD for its uses in building insulation, textile back coatings, and HIPS applications, and identified flame retardant alternatives as well as alternative forms of insulation to the use of HBCD in building insulation. This EPA report provides new and updated information on chemical flame retardant alternatives to HBCD in its primary use as a flame retardant for insulation foam.

1.2 Purpose of the Flame Retardant Alternatives Assessment

The purposes of this assessment are to: (1) identify viable alternatives for HBCD in EPS and XPS; (2) evaluate the human health and environmental profiles of HBCD and its alternatives; and (3) inform decision making as organizations choose safer alternatives to HBCD. Within DfE Alternatives Assessments, chemicals are not ranked for preferability, rather the information provided is intended for use by decision-makers, who will combine our assessment with other information to inform the selection of safer, more sustainable alternatives.

1.3 Scope of the Flame Retardant Alternatives Assessment

The Action Plan issued for HBCD in 2010 called for EPA to conduct a DfE multi-stakeholder alternatives assessment to aid users in selecting safer alternatives to HBCD.

Since the primary use for HBCD is for EPS and XPS foam insulation, the project scope did not include alternatives to HBCD for its minor uses in textile back coatings and HIPS used in electronics housings and focused on primary uses. Stakeholders interested in alternatives for these uses may refer to DfE's Partnership on Alternatives to Decabromodiphenyl Ether (decaBDE).[4] The decaBDE report considers alternative flame retardants for a wider range of polymers and applications, including electronics housings and textiles, for which both decaBDE and HBCD have been used in the past.

The assessment provides hazard information (human toxicity, ecotoxicity, environmental fate) on flame retardants that were selected for evaluation in this report as potentially viable alternatives to HBCD. Viable alternatives are those that may have similar performance and function to HBCD when used in EPS and XPS building insulation. While the assessment will not attempt to include comprehensive life-cycle assessment (LCA) information, it will, by both inclusion and reference, note relevant life-cycle considerations, describe other relevant information, and provide a general overview of potential alternative materials that may aid in the selection of alternatives to insulation containing HBCD. An in-depth comparison of potential human health and environmental impacts was not done for the alternative insulation materials described in Section 5.2. The information provided by this Partnership will help stakeholders select preferable alternatives to HBCD; however, the report will not recommend specific flame retardants or alternative materials.

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[4] http://www.epa.gov/dfe/pubs/projects/decaBDE/index.htm

The report is organized as follows:

- **Chapter 1** *(Introduction)*: This chapter provides background on the Flame Retardant Alternatives to HBCD project, including the purpose and scope of the Partnership and of this report.

- **Chapter 2** *(HBCD Uses, End-of-Life, and Exposure)*: This chapter describes the insulation products in which HBCD is used and the potential associated exposure pathways along each stage of the life cycle of the flame retardant in the products.

- **Chapter 3** *(Background on Flame Retardants)*: This chapter describes chemical flame retardants generally, as well as those specific to this assessment and provides technical information about flammability standards.

- **Chapter 4** *(Hazard Evaluation of HBCD and Alternatives)*: This chapter explains the chemical assessment method used in this report and summarizes the assessment of hazards associated with each flame retardant chemical.

- **Chapter 5** *(Summary of Hazard Assessments, Considerations for Selecting Flame Retardants and an Overview of Alternative Materials)*: This chapter includes a summary of the human health, environmental, social, performance, and cost considerations for selecting alternative flame retardants. It also includes an overview of information on alternative insulation materials, although the Partnership does not provide a direct comparison of these materials to EPS and XPS foam.

1.4 DfE Alternatives Assessments as a Risk Management Tool

Among other actions, the Agency chose to conduct a DfE Alternatives Assessment as a risk management tool for HBCD in EPA's HBCD Action Plan. The Agency chose this tool to inform the chemical substitution that may occur as an outcome of other activities described in the Action Plan. DfE Alternatives Assessments provide information on the environmental and human health profiles of chemicals that may be used as substitutes so that industry and other stakeholders can use this information, in combination with analysis of cost, performance, and other factors, to make informed choices about alternatives.

DfE Alternatives Assessments along with LCAs, risk assessments, and other tools can be used to improve the sustainability profiles of chemicals and products. These tools, which can be complementary, should be selected according to the risk management need. DfE Alternatives Assessments establish a foundation that other tools can build on.

The focus of this DfE Alternatives Assessment report is to compare the intrinsic properties of chemicals within the same functional use group (e.g., *solvent, surfactant, flame retardant, ink developer*) and to evaluate alternatives across a consistent and comprehensive set of hazard endpoints. Information about chemical hazards derived from this type of comparative chemical hazard assessment can be used by decision-makers to help them select safer alternative chemicals.

Risk assessment and DfE Alternatives Assessment are both based on the premise that risk is a function of hazard and exposure. Risk assessment characterizes the nature and magnitude of hazard and exposure from chemical contaminants and other stressors.

DfE's "functional use" approach to alternatives assessment orients chemical evaluations within a given product type and functionality. Under this approach, factors related to *exposure scenarios*, such as physical form and route of exposure, are generally constant within a given functional use analysis and would fall out of the comparison. DfE Alternatives Assessments consider intrinsic properties of chemical substitutes that affect *exposure potential*, including absorption, persistence, and bioaccumulation. Under this approach, the health and environmental profiles in the alternatives assessments become the key variables and sources of distinguishing characteristics. Exposure attributes, including significant differences in environmental fate and transport based on persistence, bioaccumulation, and physical properties, are considered and discussed in Chapters 4 and 5.

DfE Alternatives Assessments are most useful in identifying safer substitutes when available alternatives meet performance requirements and are expected to present lower hazards for human health and the environment. During decision-making, risk assessment or LCA could be applied to the lower-hazard or potentially preferable alternatives to complement the alternatives assessment findings. Alternatives assessments can also identify the characteristics of a safer alternative and guide innovation and product development, especially when clearly preferable alternatives are not available.

The DfE Alternatives Assessment approach is aligned with green chemistry principles.[5] The relationship to two of those principles is especially noteworthy:

- Principle 4: *Designing Safer Chemicals* -- "Design chemical products to affect their desired function while minimizing their toxicity," and
- Principle 10: *Design for Degradation* -- "Design chemical products so they break down into innocuous products that do not persist in the environment."

DfE incorporates these two green chemistry principles and applies them in its assessment of chemical hazard and fate in the environment. This approach enables identification of safer substitutes that emphasize greener chemistry and points the way to innovation in safer chemical design where hazard becomes a part of a performance evaluation.

[5] http://www.epa.gov/sciencematters/june2011/principles.htm

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2 HBCD Uses, End-of-Life, and Exposure

Hexabromocyclododecane (HBCD) is most commonly used in expanded polystyrene foam (EPS) and extruded polystyrene foam (XPS) produced for the building and construction industry to meet fire safety standards. HBCD also has minor uses as a flame retardant in textile back coatings and high-impact polystyrene (HIPS) used in electronics housings. As stated in Chapter 1, this alternatives assessment focuses on HBCD in EPS and XPS foam insulation and does not include alternatives to HBCD for its uses in textile back coatings and HIPS. Information on flame retardants in textile back coatings and HIPS can be found in Design for the Environment (DfE)'s Partnership on Alternatives to Decabromodiphenyl Ether (decaBDE)[6].

Chapter 2 presents the uses of HBCD with descriptions of EPS and XPS (Section 2.1), an overview of end-of-life scenarios for insulation (Section 2.2), and a summary of information pertaining to human and environmental exposure to HBCD (Section 2.3).

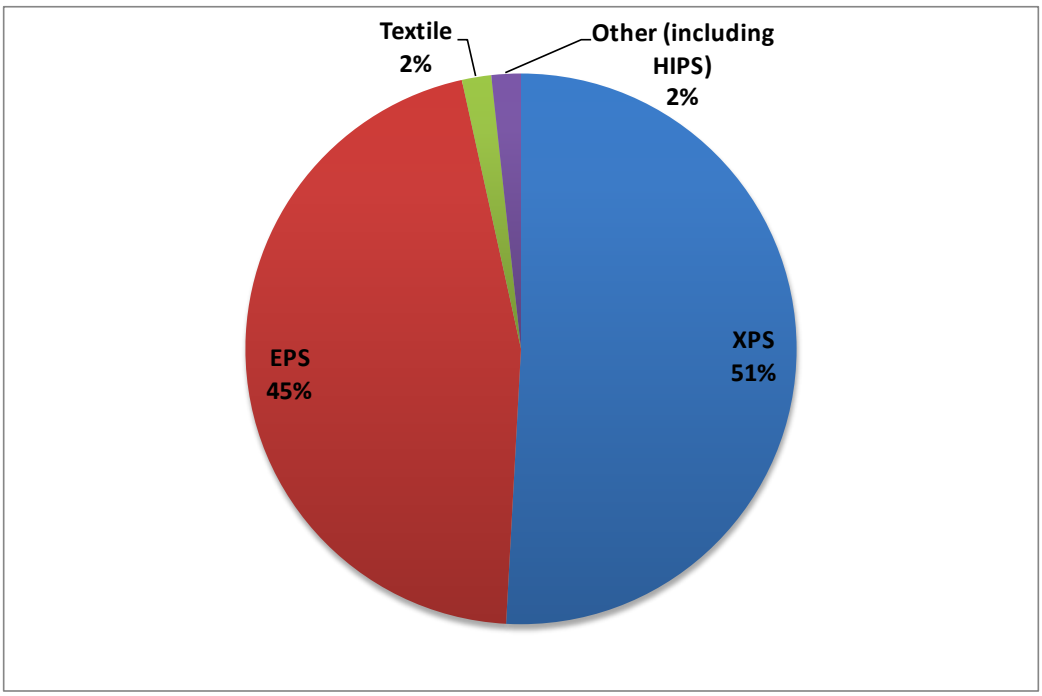
2.1 Uses of HBCD

Figure 2-1 shows the proportions of HBCD use in polystyrene foam, textile back coatings and HIPS in the European Union (EU). In 2001, the world market demand for HBCD was 16,700 tons, or 33.4 million pounds, 57% of which was attributed to Europe (Janak, Covaci et al. 2005). According to the Toxic Substances Control Act (TSCA) Inventory Update Reporting (IUR), a volume between 10 and 50 million pounds of HBCD was manufactured or imported in the U.S. in 2005 (U.S. EPA 2006). In the most recent TSCA reporting for 2011, now called Chemical Data Reporting (CDR), the volume of HBCD manufactured or imported in the U.S. was claimed confidential and cannot be described in this report (U.S. EPA 2013). More precise data for HBCD uses are available for the EU, where 96% of HBCD is used in EPS and XPS foam. Figure 2-1 reflects data for European markets, as similar information for the U.S. is not available. Although the EU market and industry for HBCD are considered to be similar to those in the U.S., differences do exist in building technologies, climate, and consumption patterns, limiting the comparison of the two markets.

The application of HBCD in EPS and XPS is discussed in Section 2.1.1 of this assessment; Section 2.1.2 provides a summary of the minor uses of HBCD in textiles and HIPS.

[6] www.epa.gov/dfe/pubs/projects/decaBDE/index.htm

Figure 2-1. Profile of HBCD Uses in European Markets for 2006/2007



(European Chemicals Agency 2009)

2.1.1 Building and Construction

Important properties of EPS and XPS include their energy efficiency, long-term performance (50-100 years), compressive strength, high moisture resistance and resistance to water absorption, versatility, durability, reusability, imperviousness to mold growth and microbiological, degradation, availability, and cost-effectiveness (EPS Industry Alliance 2011a; Extruded Polystyrene Foam Association 2011a; Fabian 2011).

EPS and XPS are used in buildings for insulation as well as to provide a moisture barrier, protect against damage from freezing, provide a stable fill material, and create high strength composite materials (Morose 2006). Typical applications include insulation in: attics, ceilings, roofs, walls, flooring, below grade applications, transportation, and cold storage (EPS Industry Alliance 2009a; EPS Industry Alliance 2011b; Extruded Polystyrene Foam Association 2011a; Extruded Polystyrene Foam Association 2011b). Other uses of polystyrene foam in consumer products (e.g., packaging) generally do not require the use of a flame retardant (European Commission 2008; EPS Industry Alliance 2011b). The use of HBCD in non-insulation applications of polystyrene foam was outside the scope of this alternatives assessment and was not researched.

Performance requirements for EPS and XPS foam used as thermal insulation are governed by American Society for Testing and Materials (ASTM) C578, *Standard Specification for Rigid, Cellular Polystyrene Insulation*.[7] In general, the performance requirements of foam insulation vary depending on the density of the foam. The ASTM C578 standards differentiate between classifications of insulation foam based on density and compressive strength. Table 2-1 below gives a broad range of properties covering the breadth of foam densities and compressive strengths cited in ASTM C578. The requirements are defined as follows:

- **Density:** Mass per unit volume.
- **R-value:** Thermal resistance. Higher R-values indicate a better ability to resist the flow of heat.
- **Compressive strength:** The compaction force (load per unit area) a material can withstand for a given change in dimensions (typically 10% reduction in thickness).
- **Flexural strength:** The breaking load applied to the neutral axis of a beam.
- **Water vapor transmission rate:** The steady state water vapor flow in unit time through unit area of a body, normal to specific parallel surfaces, under specific conditions of temperature and humidity at each surface.
- **Water absorption:** Percentage, by volume, of water remaining within the specimen after immersion in water for a specified time.
- **Dimensional stability:** The ability of a material to maintain its original size, shape, and dimensions in response to thermal and humid aging.
- **Oxygen index:** The percent of oxygen necessary to support combustion of a polymer.

Typical Applications of EPS and/or XPS:

- Attics and Ceilings
- Roofs
  - Membrane roofs
  - Recovery/reroofing
  - Vegetative roofs
- Walls
  - Continuous insulation
  - Exterior Insulating and Finishing Systems (EIFS)
  - Garage door panels
  - Insulating Concrete Forms (ICFs)
  - Masonry cavity walls
  - One-coat stucco panels
  - Precast concrete
  - Steel Stud insulation
  - Structural Insulated Panels (SIPs)
- Flooring
- Below grade applications
  - Frost Protected Shallow Foundations (FPSF)
  - Geofoam
  - Geotechnical fill & stabilization
  - Highway insulation
- Cold Storage/Low temperature buildings
- Transportation
  - Recreational vehicle panels
  - Shipping containers

(EPS Molders Association, 2009a, 2011b; Extruded Polystyrene Foam Association, 2011a, 2011b)

[7] Likewise, ASTM D6817 applies to polystyrene foams in geotechnical engineering applications ("geofoam"). See http://www.astm.org/Standards/D6817.htm.

- **Flame spread index:** The index rate expressed in distance and time at which a material will propagate flame on its surface.
- **Smoke development index:** An index indicating the potential for smoke generation during fire propagation.

Table 2-1. ASTM C578 Requirements for EPS and XPS Foam

	Unit	EPS	XPS
Classification Type		XI, I, VIII, II, IX, XIV, XV	XII, X, XIII, IV, VI, VII, V
Minimum Density	lbs per ft^3 (pcf)	0.70, 0.90, 1.15, 1.35, 1.80, 2.40, 3.00	1.20, 1.30, 1.60, 1.55, 1.80, 2.20, 3.00
Compressive strength	lbs per in^2 (psi)	5.0, 10.0, 13.0, 15.0, 25.0, 40,0, 60.0	15.0, 15.0, 20.0, 25.0, 40.0, 60.0, 100.0
Performance Requirement			
R-value	F-ft^2-h/BTU (75°F)	3.1-4.3	4.6-5
Flexural strength	lbs per in^2 (psi)	10-75	40-100
Water vapor transmission rate	Perm per inch	2.5-5.0	1.1-1.5
Water absorption	%	2.0-4.0	0.3-1.0
Dimensional Stability	%	2	2
Oxygen index	%	>24	>24
Flame spread index	Unitless index	<75	<75
Smoke development index	Unitless index	<450	<450

(International Code Council 2011a; International Code Council 2011b; American Society for Testing and Materials 2012)

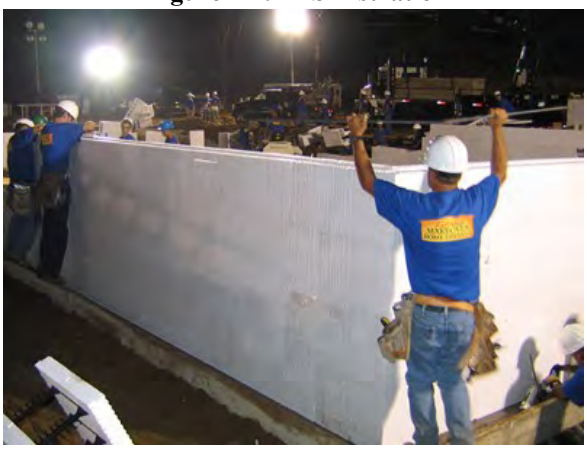
To help ensure safety of occupants, building codes in the U.S. require use of materials that reduce the risk of fire. Flame retardants are used in EPS and XPS to raise ignition temperatures and to reduce the rate of burning, flame spread, and smoke, in turn potentially allowing building occupants more time to escape a life-threatening fire. HBCD is used because of its ability to impart flame retardancy at low concentrations (at a typical loading of 0.5% by weight in EPS (EPS Industry Alliance 2009b), 0.5-1% by weight in XPS (Extruded Polystyrene Foam Association 2011a), without the loss of thermal and physical property performance. HBCD is compatible with both EPS and XPS manufacturing processes (described in more detail below). Other valued characteristics include its low water solubility and retention in the foam, such that its fire safety contribution is maintained for decades, even after extended water contact (EPS Industry Alliance 2011a; Extruded Polystyrene Foam Association 2011a; Fabian 2011). Alternatives to HBCD in EPS and XPS foam must be able to meet fire safety and other regulatory requirements while avoiding negative impacts on human health and the environment, maintaining the thermal and physical properties of the material, being compatible with manufacturing processes, and being economically viable (EPS Industry Alliance 2011a; Extruded Polystyrene Foam Association 2011a; Fabian 2011). The EPS industry is making efforts to move away from the use of HBCD in building products and to implement alternatives by developing a test program to ensure that a new polymeric flame retardant complies with building code fire performance requirements for EPS applications in Canada and the U.S. (EPS Industry Alliance 2012). After commercial quantities of alternatives become available, in-house testing and quality control measures will be independently verified through third-party certification programs (EPS Industry Alliance 2012; ICC Evaluation Service 2012).

The remainder of this section discusses the manufacturing processes used to make EPS and XPS foam containing HBCD.

Manufacture of Expanded Polystyrene (EPS)

EPS is a rigid foam insulation produced by expansion and molding of expandable polystyrene resin beads. To manufacture EPS, first a polystyrene resin is produced via suspension polymerization by chemical manufacturers. Suspension polymerization is a polymerization process that uses agitation and suspending agents to suspend monomer and polymer particles (U.S. EPA 1997). The production of EPS resin beads for insulation is done by a limited number of chemical companies at a small number (<5) of production sites in the U.S. HBCD and a blowing agent, usually pentane, are added to the resin during the polymerization process. Synergists are often used with HBCD in EPS foam to allow the concentration of HBCD to be reduced, as is discussed in more detail below. There is also a less economical two-step technology for manufacturing EPS resin that for the most part has been replaced with the one-step process described here (Grant 2011).

Figure 2-2. EPS Insulation



The expandable resin is sold and transported to molders to create EPS foam. At the molding plant, the polystyrene resin is first expanded into foam beads via the direct application of steam, which causes the blowing agent in the resin to expand. Following an aging/maturing step of approximately 2 to 24 hours, the expanded foam beads are molded into rigid closed-cell foam. This process produces blocks of foam which are cut to desired shapes (such as insulation board) and thicknesses with hot wires (COWI 2011; EPS Industry Alliance 2011a). Alternatively, the expanded foam beads may be molded into custom shapes to produce rigid foam construction elements, such as ICFs. This process typically takes place at temperatures of 120°C (COWI 2011) or below. Trim scrap from the cutting operation can be recycled into the molding operation under controlled conditions while maintaining required properties. Molding plants are typically strategically located around the country to minimize the shipping costs of transporting the lightweight foams to end users. Additional information and resources regarding EPS foam and its manufacture may be found from chemical manufacturers, processors and formulators, and industrial association websites.

Manufacture of Extruded Polystyrene (XPS)

XPS is a rigid foam insulation board produced by an extrusion process. To manufacture XPS, polystyrene resin granules and additives, including blowing agents (typically hydrofluorocarbons (HFCs)) and flame retardants (i.e., HBCD), are mixed in an extruder. The resulting mixture is melted at high pressure and high temperatures (ranging from 180-230°C) into a viscous plastic fluid. Due to these high processing temperatures, HBCD is stabilized with chemical additives to limit effects of any HBCD decomposition during manufacture, as is discussed in more detail below. Next, the viscous fluid is forced through a die, expanded into a foam and shaped. The foamed mixture is cooled into continuous sheets (boards) of closed-cell insulation. The boards are cut to size and production waste is reprocessed (Wilson 2005; COWI 2011; Extruded Polystyrene Foam Association 2011a; Fabian 2011). Additional information and resources regarding XPS foam and its manufacture may be found from chemical manufacturers, processors and formulators, and their industrial association websites.

Figure 2-3. XPS Insulation

Synergists and Stabilizers used with HBCD in EPS and XPS

Synergists are often used with HBCD for the manufacture of EPS and stabilizers are used with HBCD in the manufacture of XPS. The Partnership discussed these additives but U.S. Environmental Protection Agency (EPA) did not include them in the hazard assessment (see Chapter 4) for several reasons: the additives were outside of the project scope that focuses on alternatives to HBCD; a comprehensive hazard assessment would require inclusion of the many different additives (beyond only synergists and stabilizers) that may be present in EPS and XPS foam; and as the transition to HBCD alternatives has not yet occurred, there is not certainty as to the synergists and stabilizers likely to be used with the alternatives. However, users of HBCD alternatives are encouraged to conduct hazard assessments on additives used with flame retardants to select the safest functional chemistries. The paragraphs that follow provide general information about synergists and stabilizers used with HBCD in EPS and XPS foam, respectively.

In EPS foam, synergists are often used along with HBCD for economic reasons, as they enable the concentration of HBCD to be reduced (Arch 2011). Synergists are typically added to the EPS resin by the EPS resin manufacturer; HBCD is generally not sold with synergists added. Common synergists used with HBCD in EPS foam are:

- 2,3-dimethyl-2,3-diphenyl butane (sold as Perkadox 30); and,
- dicumyl peroxide.

Synergists are typically not used with HBCD in XPS foam because most types (e.g., peroxides) are unstable at the high processing temperatures of the XPS manufacturing process (Arch 2011).

As was noted above, HBCD must be stabilized during the XPS manufacturing process because it may decompose at the high processing temperatures. Chemical manufacturers sell a stabilized grade of HBCD for use in the XPS manufacturing process. Commonly used thermal stabilizers for HBCD in XPS foam are:

- hydrotalcite;
- dibutyl tin maleate; and
- zeolites.

Other chemicals that have been proposed in the literature as stabilizers for XPS foam include:

- aminocrotonic acid esters;
- epoxy derivatives;
- metals;
- organotins;
- polymeric acrylic binders; and
- talc.

(Hahn, Hinselmann et al. 1981; Books and Landry 1998; Hallenback, Doumen et al. 2001; Maxwell 2008; Stobby 2008; Weil and Levchik 2009).

The formulations of stabilizers in the literature ranged from 0.1 to 30 weight percent based on the weight of the flame retardant (Hahn, Hinselmann et al. 1981; Books and Landry 1998; Hallenback, Doumen et al. 2001; Maxwell 2008; Stobby 2008). Available product literature about the butadiene styrene brominated copolymer indicates that the same stabilizers used with HBCD may also be used with the alternatives (Great Lakes Solutions 2011).

2.1.2 Other Uses

The remainder of this section includes information on the uses of HBCD in textiles and HIPS. Although the report only assesses alternatives for HBCD in insulation, this information is provided as background for the reader.

HBCD in Textiles

In the U.S., producers reported that less than 1% of the total HBCD used for commercial and consumer purposes in 2005 was used in the fabrics and textiles sector (U.S. EPA 2012). Based on information submitted to EPA, it is likely that HBCD use in textiles in the U.S. is restricted to use by the automotive industry and use in non-consumer textile applications (e.g., institutional, military, and aviation), such as firefighters' suits (U.S. EPA 2012). EPA has proposed a Significant New Use Rule (SNUR) under TSCA Section 5(a)(2), which would designate the manufacture (which includes import) or processing of HBCD for use in consumer textiles as a significant new use, requiring manufacturers, importers and processors to notify EPA before manufacturing or processing HBCD for this use. In the EU, only 2% of HBCD is used in textile back coatings in applications such as flat and pile upholstered furniture, upholstery seating in

transportation, draperies, wall coverings, and automobile interior textiles and car cushions (European Chemicals Agency 2009).

The global automotive industry uses HBCD in floor mats, roof interior coverings, and other interior fabrics of motor vehicles (U.S. EPA 2012). Additionally, in Europe it has been noted that EPS may be used in children's car seats or for insulation for transport vehicles (European Commission 2008). The EPS used in children's car seats may contain HBCD, as is evidenced by the bromine content found in tested car seats (Gearhart, Posselt et al. 2008). Some automakers plan to phase out these uses of HBCD in 2015, due to the addition of HBCD to the Annex XIV List of Substances Subject to Authorisation under the EU's Registration, Evaluation, Authorisation and Restriction of Chemical Substances (REACH) regulations.

For use in textiles, HBCD is formulated into polymer-based dispersions (e.g., acrylic or latex) of variable viscosity, which are then processed in the textile finishing industry (Harscher 2011). As HBCD is applied to textiles as a surface coating, it may be released during textile wear and washing (European Commission 2008). Antimony trioxide is often used as a synergist in combination with HBCD in the flame retardation of textiles (European Commission 2008). The typical loading of HBCD in textile back coatings is 10-25% (Harscher 2011).

The use of HBCD in textile back coatings is a source of HBCD in the environment. HBCD is expected to have greater mobility from textile coatings, where it is used in a surface coating, compared to EPS and XPS, where it is dispersed throughout the polymer matrix (European Commission 2008). Additionally, the HBCD particle size for textile applications is smaller than that used for insulation, which poses the potential of deep lung particulate exposure (Rozman and Klaassen 2001). The EU risk assessment of HBCD published in 2008 (European Commission 2008) estimated releases of HBCD during its production, formulation, and use in EPS, XPS, textiles, and HIPS. These estimates indicated that textile-related releases may constitute a significant share (approximately 86%) of total HBCD releases to the environment, however, textiles only accounted for 11% of the overall use of HBCD in Europe at the time of the study (European Commission 2008). Thus, EPS, XPS, and HIPS applications of HBCD only represented 14% of the releases despite accounting for 89% of the HBCD used. Industry information indicates that the use of HBCD in textiles in Europe has declined in recent years to 2% of total HBCD use (see Figure 2-1) (IOM Consulting 2009). For information on potential alternatives to HBCD in textile back coatings, refer to *An Alternatives Assessment For The Flame Retardant Decabromodiphenyl Ether (DecaBDE)*[8], which assessed alternatives for this use.

HBCD in HIPS

The use of HBCD in HIPS accounts for approximately 2% of HBCD usage in the EU (European Chemicals Agency 2009). Similar data for the U.S. are not available. HBCD is used as a flame retardant in HIPS enclosures for audio/video equipment and other appliances, typically in "Glow Wire" and Underwriters Laboratories (UL) 94 V2 rated applications (Harscher 2011). The use of

[8] www.epa.gov/dfe/pubs/projects/decaBDE/index.htm

HBCD in these products allows for lower load levels, lower specific gravity, and non-antimony trioxide formulations (Harscher 2011). To use HBCD in HIPS, HIPS pellets are mixed with HBCD and other ingredients in an extruder; the resulting pellets then undergo granulation processes (European Commission 2008). The typical loading of HBCD in HIPS is 1-7% (European Commission 2008). For information on potential alternatives to HBCD in HIPS, refer to *An Alternatives Assessment For The Flame Retardant Decabromodiphenyl Ether (DecaBDE)*[9], which assessed alternatives for this use.

2.2 End-of-Life Scenarios

There are multiple end-of-life pathways for insulation products including reuse, recycling, landfilling or incineration. The manner in which a product is handled after use contributes to its environmental and human health impacts. The following sections consider end-of-life issues for insulation materials containing HBCD. As insulation boards comprise the majority of waste containing HBCD (Dawson 2011), they are the focus of this section.

For insulation materials, the end-of-life usually occurs when the building is altered, demolished (U.S. Department of the Interior n.d.), or burned down. During demolition, HBCD may be released in dust (European Commission 2008; Sall 2010). Common demolition techniques include implosion with explosives, use of a crane and wrecking ball, or deconstruction of the structure (European Commission 2008). Construction and demolition (C&D) debris in the U.S. is estimated to total approximately 160 million tons per year (U.S. EPA 2009). The amount of XPS and EPS insulation in this waste is unknown. In Europe, HBCD use in insulation began in the 1980s; therefore, the volume of waste containing HBCD is expected to increase after 2025, as buildings containing insulation flame retarded with HBCD are refurbished or demolished (Sall 2010).

Additionally, in some cases, insulation used on or under the soil may be left in the environment after use. For example, polystyrene insulation may be used under parking decks, rails, roads, or exterior insulation of cellars (European Commission 2008). Insulation used for these purposes often remains in the ground after its intended use is over (European Commission 2008).

The Agency's concern about HBCD stems largely from its persistent, bioaccumulative, and toxic (PBT) characteristics. HBCD bioaccumulates and biomagnifies in the food chain (U.S. EPA 2010). Along with its high toxicity towards aquatic organisms, it persists and is transported long distances in the environment and is associated with human health concerns (U.S. EPA 2010).

2.2.1 Reuse and Recycling

The end-of-life for EPS and XPS often comes when buildings are demolished or altered. However, EPS and XPS insulation may remain functional as insulation even after a building is taken out of service. Polystyrene insulation can therefore be salvaged and reused, although the board must be protected and not broken during removal (Wilson 2005; U.S. Department of the

[9] www.epa.gov/dfe/pubs/projects/decaBDE/index.htm

Interior n.d.). For example, during the re-roofing of the Dallas Fort Worth International Airport, approximately 90% of existing XPS material had maintained its thermal and physical properties over the past 17 years and was reused (Owens Corning 2007).

Additionally, polystyrene insulation board may be recycled into new polystyrene boards or other applications (European Commission 2008; Sall 2010). Polystyrene is easier to recycle compared to other foam insulation materials because it can be melted and reformed with minimal chemical modification (U.S. Department of the Interior n.d.). To do so, the polystyrene is melted and re-expanded into insulation or packaging (Wilson 2005). For example, used EPS insulation boards may be ground up and molded with virgin EPS to form new boards (European Commission 2008). Similarly, XPS may also be melted and reused in the manufacture of new insulation board (Herrenbruck n.d.). Due to the use of flame retardants (i.e., HBCD), as well as the dust and dirt accumulated during use and removal, used EPS and XPS can typically only be recycled into building insulation, and cannot be recycled into non-building applications, such as packaging (U.S. Department of the Interior n.d.). Although there is some recycling of polystyrene insulation in Europe – for example, Germany collects used polystyrene and recycles it into building insulation on a national level (European Commission 2008) – it is unclear to what extent the recycling of EPS and XPS takes place in the U.S. (Herrenbruck n.d.).

2.2.2 Landfilling

In the U.S., the majority of C&D waste is disposed of in municipal solid waste landfills or C&D landfills (U.S. EPA 1998; Dawson 2011; Sustainable Sources 2012). In landfills, weathering and degradation (via UV light, microorganisms, and physical impact) will cause these materials to release HBCD over time to the soil, and to a lesser extent to water and air (European Commission 2008; Environment Canada 2011b). However, HBCD is expected to remain largely immobile in landfills, due to its tendency to sorb to organic matter in particles and its low water solubility (Environment Canada 2011a). Therefore, the potential for groundwater contamination from landfill seepage is unlikely due to HBCD's physical-chemical properties and evidence that the chemical may undergo anaerobic biodegradation (Environment Canada 2011b).

2.2.3 Incineration

Insulation boards containing HBCD may also be incinerated, although this process is not commonly used in the U.S. (Herrenbruck n.d.). Although HBCD should be destroyed at the high temperatures found in properly functioning incinerators, releases of potentially hazardous combustion by-products such as polybrominated dibenzo-p-dioxins and dibenzofurans may occur from uncontrolled burns, accidental fires, and improperly functioning incinerators (Birnbaum, Staskal et al. 2003; Weber and Kuch 2003; Environment Canada 2011b). Recent studies also show that HBCD-containing EPS and XPS can be incinerated in advanced municipal solid waste incinerators with a very high destruction efficiency for HBCD (Plastics Europe 2014).

2.3 HBCD Exposure

Exposure can occur at many points in the life cycle of a flame retardant chemical. HBCD may be released to air, water, soil, and sediment during manufacture, processing, transportation, use,

improper handling, improper storage or containment, product usage, and disposal of the substance or products containing the substance. HBCD has also been shown to be persistent and to bioaccumulate and biomagnify in food chains (U.S. EPA 2010). Occupational exposures may occur during raw material extraction, chemical and product manufacturing, handling of material containing HBCD (e.g., handling of insulation during installation and renovation of buildings), and product end-of-life (i.e., reuse, refurbishing, recycling, incinerating, landfilling, building demolition, or fire). Consumers have the potential to be exposed to HBCD while the flame retarded product is in use (e.g., releases to the air from flame retarded textiles), however the magnitude of this exposure is highly uncertain (IOM Consulting 2009). A quantitative exposure assessment is outside the scope of this project. For an overview of exposure considerations and routes of exposure, refer to Chapter 5 of the *An Alternatives Assessment For The Flame Retardant Decabromodiphenyl Ether (DecaBDE)*. Additionally, EPA's Exposure Factors Handbook[10] provides information on various physiological and behavioral factors commonly used in assessing exposure to environmental chemicals.

2.3.1 Human Exposures

Based on the uses of HBCD, humans may be exposed during its production, industrial use, from the use of products containing HBCD, and indirectly from household dust or the environment via food, soil, water, and air (European Commission 2008). The human population can be exposed to HBCD by inhaling airborne dust, ingestion, dermal contact (European Commission 2008) and, although unlikely, by inhaling vapor. It should be noted that HBCD exposure studies generally do not compare exposure resulting from the use of flame-retarded insulation to that from other uses (e.g., textiles), however, one study did indicate that the HBCD releases from insulation are minor in comparison to textile applications (European Commission 2008).

The primary occupational exposure to HBCD is through inhaling airborne dust (European Commission 2008). Ingestion may occur as a result of inhaling dust but is not expected to be a relevant route of occupational exposure (European Commission 2008). Workers may also be exposed through dermal deposition of airborne dust or direct handling of the chemical or products during chemical and product manufacturing and during construction (European Commission 2008). For insulation applications, HBCD is typically manufactured as a standard grade powder or granule with mean particle sizes that are not respirable (European Commission 2008). However, an occupational exposure study at an industrial plant in Europe producing EPS reported measured elevated airborne dust levels and measured HBCD in the blood of workers (Thomsen, Molander et al. 2007). Occupational HBCD exposure may also occur as a result of thermal cutting of EPS and XPS at production plants and construction sites. XPS is not typically thermally cut at production plants or construction sites. When XPS is cut at production plants, fan extraction is supplied and worker exposure is mitigated due to restricted access to the area during cutting. One small-scale simulation study suggests that over 60% of the HBCD particles released during the thermal cutting of EPS and XPS would penetrate the alveolar region of a worker's lung (Zhang, Kuo et al. 2012). No readily available HBCD occupational exposure information – including biomonitoring data – was found for U.S. workers (U.S. EPA 2010).

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[10] Available at http://www.epa.gov/ncea/efh/pdfs/efh-complete.pdf.

HBCD is incorporated at high temperatures and/or pressures in EPS and XPS manufacturing. In EPS, it is dissolved chemically in styrene monomer in a reactor. In XPS, it is added to viscous, molten polystyrene in an extruder. Room temperature solid state diffusion of HBCD out of polystyrene foams would be expected to be very slow and very low. Since HBCD is an additive flame retardant, it can potentially be released from its end products over time, as it is not chemically bound to the polymer matrix (Environment Canada 2011b).

HBCD has been detected in human adipose tissue, milk, and blood and has been shown to cross the placenta (Covaci, Gerecke et al. 2006; Johnson-Restrepo, Adams et al. 2008; Meijer, Weiss et al. 2008; Arnot, McCarty et al. 2009). General population exposure to HBCD is likely from its presence in food (e.g., fish and shellfish) due to biomagnification in food chains (Heibl and Vetter 2007; Fernandes, Dicks et al. 2008; van Leeuwen and de Boer 2008), outdoor air, particularly near sites where HBCD or HBCD flame retarded materials are produced (Covaci, Gerecke et al. 2006), and indoor air (Law, Herzke et al. 2008). HBCD has also been detected in indoor dust (Covaci, Gerecke et al. 2006; Law, Herzke et al. 2008; Roosens, Abdallah et al. 2009). If HBCD is present in household (e.g., furniture upholstery) and/or automotive (e.g., textiles in vehicles) applications, children could be exposed, especially given children's increased potential exposure via dust, mouthing behavior (e.g., object-to-mouth), and hand-to-mouth ingestion pathways (U.S. EPA 2010). While biomonitoring data for HBCD in children are not available, studies of other brominated flame retardants have found higher exposures in children than adults (Center for Disease Control and Prevention 2009; Toms, Sjödin et al. 2009).

2.3.2 Environmental Exposures

HBCD is not known to occur naturally, but may be released to air, water, soil, and sediment during manufacture, processing, transportation, use, improper handling, improper storage or containment, product usage, and disposal of the substance or products containing the substance (Environment Canada 2011a). Studies suggest that a significant portion of HBCD in the environment is released from textiles. As was noted in Section 2.1.2, the EU's 2008 risk assessment of HBCD (European Commission 2008) estimated releases of HBCD during its various life-cycle stages, finding that textile-related releases may constitute a significant share (approximately 86%) of total HBCD releases to the environment in Europe. Information from the United Kingdom indicates that the primary sources of HBCD in the environment are from fugitive emissions during its manufacture and use in subsequent products, potentially from leaching in landfills, and from incinerator emissions (United Kingdom Environment Agency 2009). Because HBCD is not covalently bound to the polymer, it is possible that it may migrate out of consumer or industrial end-use products into the indoor and/or outdoor environment (Environment Canada 2011a). It should be noted that HBCD exposure studies generally do not compare exposure resulting from the use of flame-retarded insulation to exposure resulting from other uses (e.g., textiles).

Limited data are available on the degradation of HBCD in soil, water, or sediment (U.S. EPA 2010). However, HBCD has been detected in biota over large areas and in remote locations (U.S. EPA 2010). The frequent detection of HBCD over a large geographic area, with increasing occurrence in remote locations such as the Arctic, where no demonstrable local sources exist that can account for these exposures, suggests that HBCD is persistent and undergoes long-range atmospheric transport (UNEP 2009).

HBCD has been measured in air and sediment in the Arctic, Scandinavian countries, North America and Asia (Covaci, Gerecke et al. 2006; Arnot, McCarty et al. 2009; UNEP 2009). HBCD has also been measured in marine and arctic mammals, freshwater and marine fish, aquatic invertebrates, birds and bird eggs, polar bears, and one plant species (Covaci, Gerecke et al. 2006; Arnot, McCarty et al. 2009; UNEP 2009). The majority of these studies are European; some are from North America, and a few are from Asia. Additionally, studies have shown that HBCD is bioavailable and bioaccumulative (Veith, Defoe et al. 1979; Drottar, MacGregor et al. 2001; Tomy, Budakowski et al. 2004). For example, a monitoring study by De Boer et al. (2002) included a wide variety of biota (invertebrates, fish, birds, and marine mammals) and showed that HBCD bioaccumulates easily and biomagnifies in food chains.

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3 Background on Flame Retardants

This chapter includes background information on flame retardants. Section 3.1 includes background on types of flame retardants and flammability test requirements. Section 3.2 presents information regarding flame retardants for polystyrene, Section 3.3 presents the flame retardants included in this assessment, and Section 3.4 discusses those flame retardants that were considered but excluded from the assessment.

3.1 General Information on Flame Retardants

Flame retardants are chemicals used to reduce risk of fire through reducing the ignitability of materials and/or the heat generated from materials. For polymers, the simplest way, in theory, of decreasing flammability is to design the polymer so that it is thermally stable. Thermally stable polymers are less likely to decompose into combustible gases under heat stress and thus often have higher ignition resistances. Because thermally stable polymers are often difficult and expensive to process, manufacturers use other means, such as adding flame retardant chemicals, to impart flame retardant properties to materials. Since there are a large number of flame retardants on the market and they often can be a cost-effective solution for providing fire safety, these chemicals are used in a broad range of products.

As plastics have become an integral part of modern life, fire risk is perceived to be elevated because plastics can burn hotter and faster than traditional materials such as wood (Underwriters Laboratories 2012). Flame retardants, which are often added to meet flammability standards, inhibit combustion and therefore contribute to a reduced fire risk when added to flammable plastics. However, some flame retardants are associated with environmental hazards e.g., polybrominated diphenyl ethers (PBDEs) (U.S. EPA 2003b; U.S. EPA 2003a; U.S. EPA 2004; U.S. EPA 2008; U.S. EPA 2012) and contribute to hazardous by-products from a smoldering or fully engaged fire (e.g., carbon monoxide and smoke (Nelson 1998; Peck 2011)) when inhibiting combustion. Some halogenated flame retardants will yield additional hazardous by-products (e.g., halogenated dioxins and furans) during incomplete combustion (Sidhu, Morgan et al. 2013). This incomplete combustion is too complex and variable for all potential combustion by-products to be adequately included in this report. Both halogenated and non-halogenated flame retardants may yield other toxic by-products that have not been identified in this report.

The use of flame retardants can be viewed as a risk-risk trade-off. Plastic product manufacturers are challenged with using chemical additives that reduce fire risk and may increase environmental risk. There are two risk reduction arguments put forth by the stakeholders of this Partnership. They are summarized here in simple terms: (1) flame retardants reduce fire risk and reduce smoke and toxicity caused by uninhibited fires thus enabling the use of beneficial plastic products, and (2) flame retardants increase environmental risk because they release from plastics into house dust and contribute to the toxicity of combustion by-products when they burn while not significantly increasing egress time from buildings during fires. One important approach in addressing this risk-risk trade-off is identifying the least hazardous flame retardant additives available for a given polymer-product combination. This report provides the environmental information necessary for product manufacturers to identify the flame retardants with the lowest hazard for their products. Although an analysis of fire safe assemblies that do not require

additive flame retardants is outside of the scope of this report, Chapter 5 provides a general overview of alternative insulation materials and the applications in which they may be used.

Fire occurs in three stages: (1) thermal decomposition, where the solid, or condensed phase, breaks down into gaseous decomposition products as a result of heat, (2) combustion chain reactions in the gas phase, where thermal decomposition products react with an oxidant (usually air) and generate more combustion products, which then propagate the fire and release heat, and (3) transfer of the heat generated from the combustion process back to the condensed phase to continue the thermal decomposition process (Hirschler 1992; Beyler and Hirschler 2002). Those flame retardants which act in the gas phase do so by interacting with substances that are volatile. To function in the gaseous phase this way, these flame retardants themselves must become volatile and react with the substances that are being released from a product in turn making the volatile substances no longer combustible. Flame retardants that act in the condensed phase do so by forming a solid char, a glassy layer that acts by isolating the substrate from combustion, which interferes with the transfer of heat from the gas phase to the condensed phase and reduces the combustibility of the gases. The primary physical mode of flame retardancy is to reduce heat generation by forming a non-combustible layer or "diluting" the organic combustible material through the generation of water vapor and preventing the continued progression of the fire (Posner and Boras 2005). Therefore, in either state, flame retardants will act to decrease the release rate of heat (Hirschler 1994), thus reducing the burning rate, flame spread, and/or smoke generation (Morose 2006a). Flame retardant modes of action are further discussed in Chapter 3 of the report Flame-Retardant Alternatives for Decabromodiphenyl Ether (decaBDE)[11].

3.1.1 Flame Retardant Classification

Flame retardants are generally incorporated throughout a polymeric material, although they can also be coated on the external surface of the polymer to form a protective barrier. Flame retardants can be broadly classified into two types according to the method of incorporation into the polymer:

- *Reactive:* Reactive flame retardants are incorporated into the polymer during compounding and will become a permanent part of the polymer structure – i.e., the chemically-bound reactive flame retardant chemicals cease to exist as separate chemical entities. Compared to an additive flame retardant, reactive flame retardants can have a greater effect on a polymer's physical-chemical properties.

- *Additive:* Additive flame retardants are also incorporated into the polymer during compounding and may interact with the polymer, but they remain as an independent chemical species. Because they are not chemically bound to the polymer, additive flame retardants have a potential to migrate out of the polymer under certain conditions over time. Therefore plastic formulators must take this into account to avoid reducing polymer fire safety or causing exposure to humans and releases to the environment. A far greater number of additive flame retardants are offered for polymers compared to the number of

[11] http://www.epa.gov/dfe/pubs/projects/decaBDE/index.htm

reactive flame retardants. Additive flame retardants are far more versatile because commodity plastics are made for many applications, not just those requiring flame retardants, and they can be incorporated into the product up until the final stages of manufacturing.

Due to the various physical and chemical properties of flame retardant chemicals, most are used exclusively as either reactive or additive flame retardants. Both reactive and additive flame retardants can significantly change the properties of the polymers into which they are incorporated. For example, they may change the viscosity, flexibility, density, electrical properties, tensile strength, and flexural strength; they may also increase the susceptibility of the polymers to photochemical and thermal degradation.

Flame retardants can also be classified into four main categories according to chemical composition (IPC 2003; Morose 2006a):

- *Halogenated*: Halogenated flame retardants are primarily based on chlorine and bromine. Hexabromocyclododecane (HBCD) and the three alternatives assessed in this report contain bromine. In 2006, brominated compounds represented approximately 18% by volume of the global flame retardant consumption (Cusack 2007). Typical halogenated flame retardants are halogenated aliphatic and aromatic compounds, halogenated polymeric materials, and halogenated paraffins. Some halogenated flame retardants also contain other elements, such as phosphorus or nitrogen. The effectiveness of halogenated additives is due to their interference with volatile substances that are created in the combustion process, decreasing their combustibility (see Section 3.2 for more detail).

- *Inorganic*: This category includes inorganic flame retardants and flame retardant synergists such as silicon dioxide, metal hydroxides (e.g., aluminum hydroxide and magnesium hydroxide), antimony compounds (e.g., antimony trioxide), boron compounds (e.g., zinc borate – which is often used as a synergist for both halogenated and non-halogenated flame retardants), and other metal compounds (molybdenum trioxide). As a group, these flame retardants represented the largest fraction (about 46-52%) of total flame retardants consumed in 2006 because they require high loading levels to impact the desired fire safety (Cusack 2007). Antimony trioxide is invariably used as a synergist for halogenated flame retardants since by itself antimony oxide has little flame retardant effect in the presence of most burning polymers. Inorganic synergists are sometimes used with HBCD.

- *Phosphorus-based*: This category represented about 16% by volume of the global consumption of flame retardants in 2006 and includes organic and inorganic phosphates, phosphonates, and phosphinates as well as red phosphorus, covering a wide range of phosphorus compounds with different oxidation states (Cusack 2007). There are also halogenated phosphate esters, often used as flame retardants for polyurethane foams or as flame retardant plasticizers, but not commonly used in electronics applications (Hirschler 1998; Green 2000; Weil and Levchik 2004). None of the potential HBCD alternatives identified in this assessment are phosphorus-based.

- *Nitrogen-based*: These flame retardants include melamine and melamine derivatives (e.g., melamine cyanurate, melamine polyphosphate). Nitrogen compounds were estimated to account for 3% of global flame retardant consumption in 2006 (Cusack 2007). Nitrogen-containing flame retardants are often used in combination with phosphorus-based flame retardants, often with both elements in the same molecule. None of the potential HBCD alternatives identified in this assessment are nitrogen-based.

3.1.2 Flammability Tests

HBCD is used as a flame retardant in polystyrene insulation foam to allow the foam to meet the fire safety requirements of various building codes, as set by national, state, county or municipal regulations. Flammability standards are developed by a variety of entities, including national regulatory agencies such as the Consumer Product Safety Commission (CPSC), state regulatory agencies such as the California Bureau of Electronic and Appliance Repair, Home Furnishings and Thermal Insulation (BEARHFTI), or for-profit companies such as Underwriters Laboratories (UL).

In the U.S., building codes are adopted at the state or municipal level and not at the federal level (Morose 2006b; Grant 2011). The American Society for Testing and Materials (ASTM) E5 committee is responsible for developing voluntary consensus fire standards for materials, products, and assemblies that are often incorporated into state or municipal regulations. Specifically, ASTM standard E84 (*Standard Test Method for Surface Burning Characteristics of Building Materials*) is the overarching flammability test for building materials in the U.S. (Harscher 2011). ASTM E84 assesses the flame spread and smoke development of building materials by employing the Steiner Tunnel Test to compare the flame spread and smoke development against standard materials (Weil and Levchik 2009; Harscher 2011). Expanded polystyrene (EPS) and extruded polystyrene (XPS) foam also generally must meet the requirements of ASTM C578 (*Standard Specification for Rigid, Cellular Polystyrene Thermal Insulation*), as well as comply with the International Building Code (IBC) and International Residential Code (IRC) (EPS Industry Alliance 2011; Extruded Polystyrene Foam Association 2011).

Other flammability tests apply to EPS and XPS insulation foam containing HBCD in specific building assemblies. A partial list of these tests includes:

- ASTM D2863 (*Standard Test Method for Measuring the Minimum Oxygen Concentration to Support Candle-Like Combustion of Plastics*)
- ASTM E119 (*Standard Test Methods for Fire Tests of Building Construction and Materials*)
- ASTM E1354 (*Standard Test Method for Heat and Visible Smoke Release Rates for Materials and Products Using an Oxygen Consumption Calorimeter*)
- Factory Mutual (FM) 4450 (*Approval Standard for Class 1 Insulated Deck Roofs*)
- FM 4470 (*Approval Standard for Single-Ply, Polymer-Modified Bitumen Sheet, Built-Up Roof (BUR) and Liquid Applied Roof Assemblies for use in Class 1 and Noncombustible Roof Deck Construction)*
- FM 4880 (*Approval Standard for Class 1 Fire Rating of Insulated Wall or Wall and Roof/Ceiling Panels, Interior Finish Materials or Coatings and Exterior Wall Systems*)

- National Fire Protection Association (NFPA) 225 (*Model Manufactured Home Installation Standard*)[12]
- NFPA 286 (*Standard Methods of Fire Tests for Evaluating Contribution of Wall and Ceiling Interior Finish to Room Fire Growth*)
- Uniform Building Code (UBC) Standard 42-1 (*Flame Spread and Smoke Development*)[13]
- UL 94 (*Standard for Safety of Flammability of Plastic Materials for Parts in Devices and Appliances Testing*)

3.2 Brominated Flame Retardants for Polystyrene

At this time, brominated flame retardants are the only commercially and technically viable options for polystyrene foam insulation. Flame retardants for EPS and XPS must be compatible with manufacturing processes, allow the material to comply with fire safety codes, and not compromise the physical properties of the foam (Environment Canada 2011; EPS Industry Alliance 2011; Extruded Polystyrene Foam Association 2011). HBCD has been the flame retardant of choice for EPS and XPS because it imparts flame retardance at low concentrations without compromising the physical properties (e.g., thermal resistance) of the foam (EPS Industry Alliance 2009; Environment Canada 2011; Extruded Polystyrene Foam Association 2011). Based on currently available technology, using non-brominated flame retardants in polystyrene foam would require much higher concentrations of the flame retardant, which can alter the physical properties of the foam (IOM Consulting 2009).

Brominated flame retardants have the ability to interact with partial oxidation reactions that occur in the gas phase during the combustion of polystyrene, which leads to the extinction of the flame (Kaspersma, Doumen et al. 2002). Bromine-containing compounds form hydrogen bromide (HBr) and prompt the formation of hydrogen gas from radical hydrogen (Beach, Rondan et al. 2008). In addition to its ability to exhibit flame retardancy in the gas phase, HBCD has also been found to aid in polystyrene degradation through condensed-phase activity (Beach, Rondan et al. 2008).

Figure 3-1. Bromine Interaction Mechanism

$$HBr + OH\bullet \rightarrow H_2O + Br\bullet$$
$$HBr + \bullet O\bullet \rightarrow OH\bullet + Br\bullet$$
$$HBr + H\bullet \leftrightarrow H_2 + Br\bullet$$
$$HBr + RCH_2\bullet \leftrightarrow RCH_3 + Br\bullet$$
$$RBr \leftrightarrow R\bullet + Br\bullet$$

Source: Kaspersma, Doumen et al. 2002

[12] Based on ASTM E84.
[13] ibid

Although all halogens are capable of capturing free radicals produced during the combustion of polystyrene, the ability to do so effectively increases with the size of the halogen (F<Cl<Br<I) (Alaee, Arias et al. 2003). Fluorinated compounds are not used as flame retardants because they are very stable and decompose at very high temperatures, delaying the activation of the flame retardant's mechanism (Alaee, Arias et al. 2003). Iodine-based compounds are also not widely used because they decompose at slightly elevated temperatures and are unstable (Alaee, Arias et al. 2003). Brominated compounds, however, have a higher trapping efficiency and lower decomposing temperature than chlorinated compounds, making them ideal components in flame retardants (Alaee, Arias et al. 2003).

3.3 Flame Retardants Included in this Assessment

With the assistance of the multi-stakeholder partnership, U.S. Environmental Protection Agency (EPA) identified three alternatives to HBCD that fit the scope of this project: viable alternatives to HBCD for use in EPS and XPS foam insulation (see Chapter 1). A list of potential alternatives to HBCD was compiled based on information in open literature (Morose 2006b; Weil and Levchik 2009; pinfa 2011) and discussion with experts in chemical manufacturing and product development in industry, government, and academia. Through these discussions, the three alternatives shown in Table 3-1 were identified as potentially viable for use in EPS and XPS. Section 3.4 discusses other flame retardants that were considered but not included in the assessment. As was discussed in Chapter 1, while the project scope does not include alternatives to HBCD for its minor uses in textile back coatings and high-impact polystyrene

Chemical Alternatives and the Toxic Substances Control Act

EPA's Design for the Environment (DfE) program is administered by the Office of Pollution Prevention and Toxics (OPPT), which is charged with the implementation of the Toxic Substances Control Act (TSCA) and the Pollution Prevention Act (PPA).

Central to the administration of TSCA is the management of the TSCA Inventory. Section 8 (b) of TSCA requires EPA to compile, keep current, and publish a list of each chemical substance that is manufactured or processed in the United States. Companies are required to verify the TSCA status of any substance they wish to manufacture or import for a TSCA-related purpose. For more information, please refer to the TSCA Chemical Substance Inventory website: http://www.epa.gov/opptintr/existingchemicals/pubs/tscainventory/basic.html

TSCA and DfE Alternatives Assessments

Substances selected for evaluation in a DfE Alternatives Assessment generally fall under the TSCA regulations and therefore must be listed on the TSCA inventory, or be exempt or excluded from reporting before being manufactured in or imported to, or otherwise introduced in commerce in, the United States. For more information see http://www.epa.gov/oppt/newchems/pubs/whofiles.htm.

To be as inclusive as possible, DfE Alternatives Assessments may consider substances that may not have been reviewed under TSCA and therefore may not be listed on the TSCA inventory. DfE has worked with stakeholders to identify and include chemicals that are of interest and likely to be functional alternatives, ***regardless of their TSCA status.*** Chemical identities are gathered from the scientific literature and from stakeholders and, for non-confidential substances, appropriate TSCA identities are provided.

Persons are advised that substances, including DfE identified functional alternatives, may not be introduced into US commerce unless they are in compliance with TSCA. Introducing such substances without adhering to the TSCA provisions may be a violation of applicable law. Those who are considering using a substance discussed in this report should check with the manufacturer or importer about the substance's TSCA status. If you have questions about reportability of substances under TSCA, please contact the Industrial Chemistry Branch at 202-564-8740.

(HIPS) used in electronics housings, stakeholders interested in alternatives for these uses may refer to the flame retardants assessed in *An Alternatives Assessment For The Flame Retardant Decabromodiphenyl Ether (DecaBDE)*[14].

Table 3-1. Summary of Chemicals for Assessment

Chemical Name	CASRN	Status
Hexabromocyclododecane (HBCD)	25637-99-4; 3194-55-6	Action Plan chemical. Included for comparative purposes.
Benzene, ethenyl-, polymer with 1,3 butadiene, brominated; "butadiene styrene brominated copolymer"	1195978-93-8	Announced by The Dow Chemical Company and Great Lakes Solutions, A Chemtura Business on March 29, 2011 (Great Lakes Solutions, A Chemtura Business 2011). The chemical has also been licensed to ICL-IP and Albemarle.
Benzene, 1,1'-(1-methylethylidene)bis[3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)]; "TBBPA-bis brominated ether derivative"	97416-84-7	Proposed as an alternative by a chemical manufacturer.
Tetrabromobisphenol A Bis (2,3-dibromopropyl) Ether	21850-44-2	This flame retardant was submitted as an alternative to HBCD to the Stockholm Persistent Organic Pollutants Review Committee (POPRC) (Lorenzi and Garlaschi 2013).

3.4 Flame Retardants Not Included in this Assessment

In addition to the chemicals listed in Table 3-1, the Partnership considered other flame retardants for the assessment, including individual chemicals and materials. Section 3.4.1 describes chemicals that were identified as possible alternatives to HBCD and the reasons they were excluded from the assessment.

3.4.1 Specific Chemicals that were Excluded from this Assessment

The chemicals listed in this section were identified as possible alternatives to HBCD, but were not included in the alternatives assessment. Reasons for exclusion included:

- The chemical is not a flame retardant, but rather a blend of flame retardants and other additives intended to improve the performance of certain flame retardants through synergistic mixtures;
- Not functional in typical EPS and/or XPS manufacturing processes; and
- Interferes with ability of EPS and/or XPS to meet building codes or flammability standards.

A summary of the chemicals that were discussed but not included in this assessment is listed in Table 3-2 along with the reason for exclusion. It is possible that there are alternatives that the Partnership was not aware of or were under development at the time this report was compiled; therefore, Table 3-1 and Table 3-2 may not list all of the possible alternatives to HBCD.

[14] http://www.epa.gov/dfe/pubs/projects/decaBDE/index.htm

Table 3-2. Chemicals Considered but Not Included in the Final Alternatives Assessment[1]

Chemical Name	CASRN	Reason for Exclusion
Brominated Flame Retardants		
Tetrabromocyclooctane	31454-48-5; 3194-57-8	This flame retardant is not functional in current EPS and XPS manufacturing processes. Its thermal stability does not meet operating temperature requirements for the manufacture of XPS foam.
Dibromoethyldibromocyclohexane	3322-93-8	Polystyrene manufacturers have noted insufficient thermal stability and an inferior persistent, bioaccumulative, and toxic (PBT) chemical assessment.
Chloropentabromocyclohexane	87-84-3	The manufacture of this flame retardant was discontinued in favor of HBCD due to an inferior environmental health and safety profile. This flame retardant may also interfere with the styrene polymerization process, resulting in a product with a lower average molecular weight (MW) and more residual unreacted styrene in the product. The resulting foam will lack the strength to meet building code requirements.
Cinnamalacetophenone tetrabromide	N/A[1]	This flame retardant was used for a time but discontinued. Its chemical structure is similar to that of 1,2-dibromoalkyl ketones. Referring to the patent literature, EPA identified this CAS name as expected to be 1-Pentanone, 2,3,4,5-tetrabromo-1,5-diphenyl-; CASRN 31611-84-4.
Hexabromohexene	125512-87-0	This flame retardant is recommended in patents as a potential alternative, but there is no information indicating that it is currently used by industry. It is also similar in structure to chloropentabromocyclohexane, so it may also interfere with the styrene polymerization process.
1,2-Dibromoalkyl ketones	N/A[1]	This flame retardant is recommended in patents as a potential alternative, but there is no information indicating that it is currently used by industry. Polystyrene foam manufacturers have observed insufficient functionality.
1,1,2,3,4,4-Hexabromo-2-butene	72108-73-7; 36678-45-2	This flame retardant is recommended in patents as a potential alternative, but there is no information indicating that it is currently used by industry. This flame retardant may also interfere with the styrene polymerization process, resulting in a product with a lower average MW and more residual unreacted styrene in the product. The resulting foam will lack the strength to meet building code requirements.
bis(2,3-dibromopropyl) tetrabromophthalate	N/A[1]	This flame retardant is not as effective per unit weight as other alkyl halides and polystyrene foam manufacturers have observed insufficient flame retardant activity. Referring to the patent literature, EPA identified this CAS name as 1,2-Benzenedicarboxylic acid, 3,4,5,6-tetrabromo-, 1,2-bis(2,3-dibromopropyl) ester; CASRN 214216-08-7.
2,4,6-Tribromophenyl allyl ether	3278-89-5	This flame retardant is recommended in patents as a potential alternative. It is not a potential alternative for the use of HBCD in XPS foam because of its poor thermal stability at operating temperatures. It is not a cost-effective alternative in EPS because it is only viable in the less-economic two-step manufacturing process. This flame retardant may also interfere with the styrene polymerization process, resulting in a product with a lower average MW and more residual unreacted styrene in the product, resulting in foam that will lack the strength to meet building code requirements.
bis(allyl ether) of tetrabromobisphenol A	25327-89-3	This flame retardant is recommended in patents as a potential alternative, but in general only has limited use and availability. It does not work well in XPS manufacturing processes, and for EPS is only viable in the less-economic two-step manufacturing process. The lower brominated content and mixture of aliphatic and aromatic bromine affects the efficiency of the material.

Chemical Name	CASRN	Reason for Exclusion
N-(2,3-dibromopropyl)-4,5-dibromotetrahydrophthalimide	93202-89-2	This flame retardant is recommended in patents as a potential alternative, but feedback from polystyrene foam manufacturers indicated problems with its use, including insufficient flame retardant activity.
Dialkyl tetrabromophthalate	N/A[1]	This flame retardant is recommended in patents as a potential alternative, but polystyrene foam manufacturers have observed insufficient flame retardant activity. It is also known to have mutagenic affects. Referring to the patent literature, EPA identified this CAS name as 1,2-Benzenedicarboxylic acid, 3,4,5,6-tetrabromo-, 1,2-bis(2-ethylhexyl) ester; CASRN 26040-51-7.
tris(2,3-dibromopropyl) phosphate	126-72-7	This flame retardant was used for a time but discontinued due to its mutagenicity.
Blends		
Aluminum Hydroxide/Alumina Trihydrate (ATH) (recommended with further addition of phosphorus or brominated FRs)	21645-51-2	This flame retardant will require high loading in EPS and XPS. It has also already been assessed in Design for the Environment (DfE)'s *An Alternatives Assessment For The Flame Retardant Decabromodiphenyl Ether (DecaBDE).*
Brominated anionic styrene polymer + bis(pentabromophenyl) ethane	N/A[1] + 84852-53-9	These blends are synergistic mixtures used to improve performance of certain FRs. They are not potential alternatives to HBCD.
Bromoaliphatic FR + a more thermally stable bromine compound with an aromatic, vinylic, or neopentyl structure	N/A[1]	
Halogenated FR + P-N compound	N/A[1]	
Elemental sulfur + phosphorus additive	7704-34-9 + 7723-14-0	
Graphite particles (halogenated FR and (optional) antimony oxide, or with a phosphorus FR)	N/A[1]	Graphite is used to increase thermal properties rather than for flame retardancy. Expandable graphite has been used as a flame retardant in some polymers but is not expected to impart flame retardancy in EPS and XPS.
Epoxy resin containing reacted-in DOPO and phosphoric acid	N/A[1]	This flame retardant is unlikely to be a functional alternative in EPS and XPS due to insufficient flame retardant activity.
Other Classes		
Nano-particle coatings	N/A[1]	At low loading levels, these nanoparticle fire retardant coatings significantly reduce polyurethane foam flammability and can result in self-extinguishing fire behavior. National Institute of Standards and Technology (NIST) is evaluating this fire retardant technology that may have potential for XPS. The EPS industry processes material with hot wires, and particles that do not melt tend to create problems during this step.
Thiophosphates and dithiophosphates	N/A[1]	Polystyrene foam manufacturers observed insufficient flame retardant activity.
Flame resistant barrier - coating, laminate, foil	N/A[1]	Back coatings may not work with polystyrene foam because they will interfere with the ability of the foam to recede away from the fire. Additionally, the coating levels necessary to pass flammability tests are not economical.
Boric acid + binder	N/A[1]	This chemical is used as a smoke suppressant rather than as a flame retardant. It should also be noted that

Chemical Name	CASRN	Reason for Exclusion
		boric acid is a substance of very high concern in the European Union (EU).
Dimethyl methyl phosphonate (DMMP)	756-79-9	This chemical is too volatile for polystyrene foam.
Hypophosphite, calcium salt (with synergists)	7789-79-9	Polystyrene manufacturers have noted insufficient flame retardant activity.
Magnesium dihydroxide	1309-42-8	This flame retardant is not viable for polystyrene foam because it is not soluble and would require high loadings. It has also already been assessed in Design for the Environment (DfE)'s Flame Retardants in Printed Circuit Boards Partnership and the Flame Retardant Alternatives for DecaBDE Partnership.

Source: Personal Communication with members of the Partnership on Flame Retardant Alternatives for HBCD.
[1] A specific CASRN was not suitable for entries that cover a general group or larger class of chemicals.

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4 Hazard Evaluation of HBCD and Alternatives

This chapter summarizes the toxicological and environmental hazards of hexabromocyclododecane (HBCD) and each of the three alternative chemicals that were identified as potential functional substitutes for HBCD. Evaluations of chemical formulations may also include associated substances (e.g., starting materials, by-products, and impurities) if their presence is specifically required to allow that alternative to fully function in the assigned role. Otherwise, pure substances were analyzed in this assessment. Users of the alternative assessments should be aware of the purity of the trade product they purchase, as the presence of impurities may alter the assessment of the alternative. This report is a hazard assessment, not a risk assessment. Hazard assessment as a risk management tool is discussed in more detail in Section 1.4.

Toxicological and environmental endpoints included in the hazard profiles are discussed in Section 4.1 along with the criteria used to evaluate each hazard endpoint. Data sources and the review methodology are described in Section 4.2. The report then offers a detailed description of the utility of physical-chemical properties in understanding hazard in Section 4.3 and the process of evaluating human health and environmental endpoints in Sections 4.4 and 4.5, respectively. A discussion of the evaluation of endocrine activity is included in Section 4.6. The characteristics of each chemical included in the alternatives assessment are summarized in the comparative hazard summary table in Section 4.7. Lastly, the collected data and hazard profile of each chemical are presented in Section 4.8.

4.1 Toxicological and Environmental Endpoints

The assessment of endpoints with the intent to create hazard profiles for a Design for the Environment (DfE) alternatives assessment follows the guidance of the *Alternatives Assessment Criteria for Hazard Evaluation* (U.S. EPA 2011b). The definitions for each endpoint evaluated following these criteria are outlined in Section 4.1.1 and the criteria by which these endpoints are evaluated are outlined in Section 4.1.2. Lastly, there are endpoints that DfE characterizes but does not assign criteria to, and these are summarized in Section 4.1.3.

4.1.1 Definitions of Each Endpoint Evaluated Against Criteria

Hazard designations for each chemical discussed in this report were made by direct comparison of the experimental or estimated data to the *DfE Alternatives Assessment Criteria for Hazard Evaluation* (U.S. EPA 2011b). Table 4-1 provides brief definitions of human health toxicity, environmental toxicity and environmental fate endpoints.

Table 4-1. Definitions of Toxicological and Environmental Endpoints for Hazard Assessment

Endpoint Category	Endpoint	Definition
Human Health Effects	**Acute Mammalian Toxicity**	Adverse effects occurring following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.
	Carcinogenicity	Capability of a substance to increase the incidence of malignant neoplasms, reduce their latency, or increase their severity or multiplicity.
	Mutagenicity/Genotoxicity	*Mutagenicity*. The ability of an agent to induce permanent, transmissible changes in the amount, chemical properties, or structure of the genetic material. These changes may involve a single gene or gene segment, a block of genes, parts of chromosomes, or whole chromosomes. Mutagenicity differs from genotoxicity in that the change in the former case is transmissible to subsequent cell generations. *Genotoxicity*. The ability of an agent or process to alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication process, or which in a non-physiological manner (temporarily) alter its replication.
	Reproductive Toxicity	The occurrence of biologically adverse effects on the reproductive systems of females or males that may result from exposure to environmental agents. The toxicity may be expressed as alterations to the female or male reproductive organs, the related endocrine system, or pregnancy outcomes. The manifestation of such toxicity may include, but is not limited to: adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, gestation, parturition, lactation, developmental toxicity, premature reproductive senescence or modifications in other functions that were dependent on the integrity of the reproductive systems.
	Developmental Toxicity	Adverse effects in the developing organism that may result from exposure prior to conception (either parent), during prenatal development, or postnatally to the time of sexual maturation. Adverse developmental effects may be detected at any point in the lifespan of the organism. The major manifestations of developmental toxicity include: (1) death of the developing organism, (2) structural abnormality, (3) altered growth, and (4) functional deficiency.
	Neurotoxicity	An adverse change in the structure or function of the central and/or peripheral nervous system following exposure to a chemical, physical, or biological agent.

Endpoint Category	Endpoint	Definition
	Repeated Dose Toxicity	Adverse effects (immediate or delayed) that impair normal physiological function (reversible and irreversible) of specific target organs or biological systems following repeated exposure to a chemical substance by any route relevant to humans. Adverse effects include biologically significant changes in body and organ weights, changes that affect the function or morphology of tissues and organs (gross and microscopic), mortality, and changes in biochemistry, urinalysis, and hematology parameters that are relevant for human health; may also include immunological and neurological effects.
	Respiratory Sensitization	Hypersensitivity of the airways following inhalation of a substance.
	Skin Sensitization	A cell-mediated or antibody-mediated allergic response characterized by the presence of inflammation that may result in cell death, following an initial induction exposure to the same chemical substance, i.e., skin allergy.
	Eye Irritation/Corrosivity	Irritation or corrosion to the eye following the application of a test substance.
	Dermal Irritation/Corrosion	Dermal irritation - reversible damage to the skin following the application of a test substance for up to 4 hours. Dermal corrosion - irreversible damage to the skin namely, visible necrosis through the epidermis and into the dermis following the application of a test substance for up to 4 hours.
Environmental Toxicity	Environmental toxicity refers to adverse effects observed in living organisms that typically inhabit the wild; the assessment is focused on effects in three groups of surrogate aquatic organisms (freshwater fish, invertebrates, and algae).	
	Aquatic Toxicity (Acute)	The property of a substance to be injurious to an organism in a short-term (days), aquatic exposure to that substance.
	Aquatic Toxicity (Chronic)	The property of a substance to cause adverse effects to aquatic organisms during aquatic exposures which were determined in relation to the life cycle of the organism.
Environmental Fate	**Environmental Persistence**	The length of time the chemical exists in the environment, expressed as a half-life, before it is destroyed (i.e., transformed) by natural or chemical processes. For alternative assessments, the amount of time for complete assimilation (ultimate removal) is preferred over the initial step in the transformation (primary removal).
	Bioaccumulation	The process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment (e.g., dietary and ambient environment sources). Bioaccumulation is the net result of competing processes of chemical uptake into the organism at the respiratory surface and from the diet and chemical elimination from the organism including respiratory exchange, fecal egestion, metabolic biotransformation of the parent compound, and growth dilution.

The hazard profile for each chemical contains endpoint-specific summary statements (see Section 4.8). For each of the endpoints listed in Table 4-1, these summary statements provide the hazard designation, the type of data (experimental or estimated) and the rationale. The endpoint summaries may also include explanatory comments, a discussion of confounding factors or an indication of the confidence in the data to help put the results in perspective.

4.1.2 Criteria

Table 4-2 summarizes the criteria that were used by DfE to interpret the data presented in the hazard profiles. The same criteria are used to evaluate hazard for all alternatives assessments conducted by DfE since 2011. These criteria, collectively known as *DfE Alternatives Assessment Criteria for Hazard Evaluation*, underwent Agency-wide and public comment, and were finalized in 2011 (U.S. EPA 2011b). A hazard designation for each human health endpoint was not given for each route of exposure but rather was based on the exposure route with the highest hazard designation. Data may have been available for some or all relevant routes of exposure.

The details as to how each endpoint was evaluated are described below and in the DfE full criteria document, *DfE Alternatives Assessment Criteria for Hazard Evaluation*, available at: http://www.epa.gov/dfe/alternatives_assessment_criteria_for_hazard_eval.pdf.

Table 4-2. Criteria Used to Assign Hazard Designations

Endpoint	Very High	High	Moderate	Low	Very Low
Human Health Effects					
Acute mammalian toxicity					
Oral median lethal dose (LD_{50}) (mg/kg)	≤50	>50–300	>300–2000	>2000	–
Dermal LD_{50} (mg/kg)	≤200	>200–1000	>1000–2000	>2000	–
Inhalation median lethal concentration (LC_{50}) - vapor/gas (mg/L)	≤2	>2–10	>10–20	>20	–
Inhalation LC_{50} - dust/mist/ fume (mg/L)	≤0.5	>0.5–1.0	>1–5	>5	–
Carcinogenicity					
Carcinogenicity	*Known or presumed human carcinogen* Equivalent to Globally Harmonized System of Classification and Labeling of Chemicals (GHS) Categories 1A and 1B	*Suspected human carcinogen* Equivalent to GHS Category 2	*Limited or marginal evidence of carcinogenicity in animals* And inadequate evidence in humans	*Negative studies or robust mechanism-based Structure Activity Relationship (SAR)* As described above	–
Mutagenicity/Genotoxicity					
Germ cell mutagenicity	GHS Category 1A or 1B: Substances known to induce heritable mutations or to be regarded as if they induce heritable mutations in the germ cells of humans	GHS Category 2: Substances which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans OR	Evidence of mutagenicity supported by positive results in *in vitro* OR *in vivo* somatic cells of humans or animals	Negative for chromosomal aberrations and gene mutations, or no structural alerts.	--

Endpoint	Very High	High	Moderate	Low	Very Low
Mutagenicity and genotoxicity in somatic cells		Evidence of mutagenicity supported by positive results in *in vitro* AND *in vivo* somatic cells and/or germ cells of humans or animals			
Reproductive toxicity					
Oral (mg/kg/day)	–	<50	50–250	>250-1000	>1000
Dermal (mg/kg/day)	–	<100	100–500	>500-2000	>2000
Inhalation - vapor, gas (mg/L/day)	–	<1	1–2.5	>2.5-20	>20
Inhalation - dust/mist/fume (mg/L/day)	–	<0.1	0.1–0.5	>0.5-5	>5
Developmental toxicity					
Oral (mg/kg/day)	–	<50	50–250	>250-1000	>1000
Dermal (mg/kg/day)	–	<100	100–500	>500-2000	>2000
Inhalation - vapor, gas (mg/L/day)	–	<1	1–2.5	>2.5-20	>20
Inhalation - dust/mist/fume (mg/L/day)	–	<0.1	0.1–0.5	>0.5-5	>5
Neurotoxicity					
Oral (mg/kg/day)	–	<10	10–100	>100	–
Dermal (mg/kg/day)	–	<20	20–200	>200	–
Inhalation - vapor, gas (mg/L/day)	–	<0.2	0.2–1.0	>1.0	–
Inhalation - dust/mist/fume (mg/L/day)	–	<0.02	0.02–0.2	>0.2	–
Repeated-dose toxicity					
Oral (mg/kg/day)	–	<10	10–100	>100	–
Dermal (mg/kg/day)	–	<20	20–200	>200	–
Inhalation - vapor, gas (mg/L/day)	–	<0.2	0.2–1.0	>1.0	–
Inhalation - dust/mist/fume (mg/L/day)	–	<0.02	0.02–0.2	>0.2	–
Sensitization					
Skin sensitization	–	High frequency of sensitization in humans and/or high potency in animals (GHS Category 1A)	Low to moderate frequency of sensitization in human and/or low to moderate potency in animals (GHS Category 1B)	Adequate data available and not GHS Category 1A or 1B	–

Endpoint	Very High	High	Moderate	Low	Very Low
Respiratory sensitization	–	Occurrence in humans or evidence of sensitization in humans based on animal or other tests (equivalent to GHS Category 1A and 1B)	Limited evidence including the presence of structural alerts	Adequate data available indicating lack of respiratory sensitization	–
Irritation/corrosivity					
Eye irritation/corrosivity	Irritation persists for >21 days or corrosive	Clearing in 8–21 days, severely irritating	Clearing in ≤7 days, moderately irritating	Clearing in <24 hours, mildly irritating	Not irritating
Skin irritation/corrosivity	Corrosive	Severe irritation at 72 hours	Moderate irritation at 72 hours	Mild or slight irritation at 72 hours	Not irritating
Endocrine activity					
Endocrine Activity	*For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.*				
Environmental Toxicity and Fate					
Aquatic toxicity					
Acute aquatic toxicity – LC_{50} or half maximal effective concentration (EC_{50}) (mg/L)	<1.0	1–10	>10–100	>100 or No Effects at Saturation (NES)	–
Chronic aquatic toxicity – lowest observed effect concentration (LOEC) or chronic value (ChV) (mg/L)	<0.1	0.1–1	>1–10	>10 or NES	–
Environmental persistence					
Persistence in water, soil, or sediment	Half-life >180 days or recalcitrant	Half-life of 60–180 days	Half-life <60 but ≥16 days	Half-life <16 days OR passes Ready Biodegradability test not including the 10-day window. No degradation products of concern.	Passes Ready Biodegradability test with 10-day window. No degradation products of concern.
Persistence in air (half-life days)	*For this endpoint, High/Moderate/Low etc. characterizations will not apply. A qualitative assessment of available data will be prepared.*				

Endpoint	Very High	High	Moderate	Low	Very Low
Bioaccumulation					
Bioconcentration Factor (BCF)/Bioaccumulation Factor (BAF)	>5000	5000–1000	<1000–100	<100	–
Log BCF/BAF	>3.7	3.7–3	<3-2	<2	–

Very High or Very Low designations (if an option for a given endpoint in Table 4-2) were assigned only when there were experimental data located for the chemical under evaluation. In addition, the experimental data must have been collected from a well conducted study specifically designed to evaluate the endpoint under review. If the endpoint was estimated using experimental data from a close structural analog, by professional judgment, or from a computerized model, then the next-level designation was assigned (e.g., use of data from a structural analog that would yield a designation of very high would result in a designation of high for the chemical in review). One exception is for the estimated persistence of polymers with an average molecular weight (MW) >1,000 daltons, which may result in a Very High designation.

4.1.3 Endpoints Characterized but Not Evaluated

Several additional endpoints were characterized, but not evaluated against hazard criteria. This is because the endpoints lacked a clear consensus concerning the evaluation criteria (endocrine activity), data and expert judgment were limited for industrial chemicals (persistence in air, terrestrial ecotoxicology), or the information was valuable for the interpretation of other toxicity and fate endpoints (including toxicokinetics and transport in the environment).

Table 4-3. Definitions of Endpoints and Information Characterized but Not Evaluated Against Hazard Criteria

Toxicological Endpoint	Definition
Toxicokinetics	The determination and quantification of the time course of absorption, distribution, biotransformation, and excretion of chemicals (sometimes referred to as *pharmacokinetics*).
Biomonitoring Information	The measured concentration of a chemical in biological tissues where the analysis samples were obtained from a natural or non-experimental setting.
Environmental Transport	The potential movement of a chemical, after it is released to the environment, within and between each of the environmental compartments, air, water, soil, and sediment. Presented as a qualitative summary in the alternative assessment based on physical-chemical properties, environmental fate parameters, and simple volatilization models. Also includes distribution in the environment as estimated from a fugacity model[1].
Persistence in Air	The half-life for destructive removal of a chemical substance in the atmosphere. The primary chemical reactions considered for atmospheric persistence include hydrolysis, direct photolysis, and the gas phase reaction with hydroxyl radicals, ozone, or nitrate radicals. Results are used as input into the environmental transport models.
Immunotoxicology	Adverse effects on the normal structure or function of the immune system caused by chemical substances (e.g., gross and microscopic changes to immune system organs, suppression of immunological response, autoimmunity, hypersensitivity, inflammation, and disruption of immunological mechanistic pathways).
Terrestrial Ecotoxicology	Reported experimental values from guideline and nonguideline studies on adverse effects on the terrestrial environment. Studies on soil, plants, birds, mammals, invertebrates were also included.
Endocrine Activity	A change in endocrine homeostasis caused by a chemical or other stressor from human activities (e.g., application of pesticides, the discharge of industrial chemicals to air, land, or water, or the use of synthetic chemicals in consumer products.)

[1]A fugacity model predicts partitioning of chemicals among air, soil, sediment, and water under steady state conditions for a default model "environment" (U.S. EPA 2012c).

4.2 Data Sources and Assessment Methodology

This section explains how data were collected (Section 4.2.1), prioritized, and reviewed (Section 4.2.2) for use in the development of hazard profiles. High-quality experimental studies lead to a thorough understanding of behavior and effects of the chemical in the environment and in living organisms. Analog approaches and SAR-based estimation methods are also useful tools and are discussed throughout this section. Information on how the alternative butadiene styrene brominated copolymer included in this assessment differs from discrete chemicals in terms of how it was evaluated is presented in Section 4.2.3.

4.2.1 Identifying and Reviewing Measured Data

For each chemical assessed, data were collected in a manner consistent with the *High Production Volume (HPV) Chemical Challenge Program Guidance* (U.S. EPA 1999b) on searching for existing chemical information. This process resulted in a comprehensive search of the literature for available experimental data. For chemicals well characterized by experimental studies, this usually resulted in the collection of recent high-quality reviews or peer-reviewed risk assessments. These were supplemented by primary searches of scientific literature published after these secondary sources were released, which is explained in greater detail below. For chemicals that are not as well characterized, that is, where these secondary sources were not available or lacked relevant or adequate data, a comprehensive search of the primary scientific literature was done. Subsequently, these searches led to the collection and review of articles from the scientific literature, industrial submissions, encyclopedic sources, and government reports. In addition, data presented in EPA public databases (e.g., integrated risk information system (IRIS); the High Production Volume Information System) and confidential databases were obtained for this project. Generally, foreign language (non-English) reports were not used unless they provided information that was not available from other sources.

Chemical assessments were performed by first searching for experimental data for all endpoints in Table 4-1. For the three alternatives assessed, high-quality secondary sources were not available; therefore, a comprehensive search of the literature was performed to identify experimental data. In some cases, confidential studies were also submitted to EPA by chemical manufacturers available to support hazard designations. For those chemicals that were expected to form stable metabolites or degradation products, searches were performed to identify relevant fate and toxicity information for the metabolite or degradation product.

Well Studied Chemicals – Literature Search Strategy

As mentioned above, for chemicals that have been well studied, limited to HBCD in this Alternatives Assessment, the literature review focused primarily on the use of secondary sources, such as Agency for Toxic Substances and Disease Registry (ATSDR) Toxicological Profiles or EPA's Integrated Risk Information System (IRIS) assessments. For HBCD, an Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS) (National Industrial Chemicals Notification and Assessment Scheme 2012), an Organisation for Economic Co-operation Development (OECD) Screening Information Dataset Initial Assessment Profile

(SIAP) from 2007 (Organisation for Economic Co-Operation and Development (OECD) 2007), a National Academy of Sciences National Research Council (National Research Council 2000) risk assessment, a European Communities (European Commission 2008; Scientific Committee on Health and Environmental Risks (SCHER) 2008b; Scientific Committee on Health and Environmental Risks (SCHER) 2008a) assessment, and a Screening Assessment by Environment Canada/Health Canada (Environment Canada 2011) were available. Using high-quality secondary sources maximized available resources and eliminated potential duplication of effort. However, more than one secondary source was typically used to verify reported values, which also reduced the potential for presenting a value that was transcribed incorrectly from the scientific literature. Although other sources might also contain the same experimental value for an endpoint, effort was not focused on building a comprehensive list of these references, as it would not have enhanced the ability to reach a conclusion in the assessment. When data for a selected endpoint could not be located in a secondary source for an otherwise well studied chemical, the primary literature was searched by endpoint and experimental studies were assessed for relevant information.

Making Predictions in the Absence of Measured Data

In the absence of primary or secondary data, hazard designations were based on (1) Quantitative Structure Activity Relationships (QSAR)-based estimations from the EPA New Chemical Program's predictive methods; (2) analog data; (3) class-based assignments from the EPA Chemical Categories document; and (4) expert judgment by EPA subject matter experts.

For chemicals that lacked experimental information, QSAR assessments were made using either EPA's Estimation Programs Interface (EPISuite™) for physical-chemical property and environmental fate endpoints or EPA's Ecological Structure Activity Relationships (ECOSAR™) QSARs for ecotoxicity. For the cancer endpoint, EPA's OncoLogic expert system was consulted, but did not provide results for HBCD or the alternatives because an appropriate chemical class was not available within the model to evaluate these chemicals. These estimation methods have been automated, and are available for free (U.S. EPA 2012d). Often analog data were used to support predictions from models. These approaches were described in the EPA Pollution Prevention (P2) Framework and Sustainable Futures (SF) program (U.S. EPA 2005b; U.S. EPA 2012c).

For some physical-chemical properties that could not be estimated using EPISuite™, such as acid/base dissociation constants, other available methods (e.g., the SPARC Performs Automated Reasoning in Chemistry (SPARC) website for dissociation constants) were used. All estimation methods employed were limited to those freely available in the public domain.

The methodology and procedures used to evaluate a polymer are described in Section 4.2.3. The endpoints for impurities and oligomers with a MW >1,000 daltons were estimated using professional judgment and the results assessed for inclusion in the overall hazard designation. This process is described, as appropriate, under the corresponding endpoints appearing in Section 4.3.

When QSAR models were not available, professional judgment was used to identify hazards for similar chemicals using the guidance from EPA's New Chemicals Categories (U.S. EPA 2010b).

The categories identify substances that share chemical and toxicological properties and possess potential health or environmental concerns (U.S. EPA 2010a). In the absence of an identified category, analogs for which experimental data are available were identified using EPA's Analog Identification Methodology (AIM) or by substructure searches of confidential EPA databases (U.S. EPA 2012a). If a hazard designation was still not available, the expert judgment of scientists from EPA's New Chemical Program would provide an assessment of the physical-chemical properties, environmental fate, aquatic toxicity, and human health endpoints to fill remaining data gaps.

4.2.2 Hierarchy of Data Adequacy

Once the studies were obtained, they were evaluated to establish whether the hazard data were of sufficient quality to meet the requirements of the assessment process. The adequacy and quality of the studies identified in the literature review are described in the Data Quality field of the chemical assessments presented in Section 4.8. The tiered approach described below represents a general preferred data hierarchy, but the evaluation of toxicological data also requires flexibility based on expert judgment.

1. One or more studies conducted in a manner consistent with established testing guidelines
2. Experimentally valid but nonguideline studies (i.e., do not follow established testing guidelines)
3. Reported data without supporting experimental details
4. Estimated data using SAR methods or professional judgment based on an analog approach
5. Expert judgment based on mechanistic and structural considerations

In general, data were considered adequate to characterize an endpoint if they were obtained using the techniques identified in the HPV data adequacy guidelines (U.S. EPA 1999b). Studies performed according to Harmonized EPA or OECD guidelines were reviewed to confirm that the studies followed all required steps.

Experimental studies published in the open literature were reviewed for their scientific rigor and were also compared and contrasted to guideline studies to identify potential problems arising from differences in the experimental design. Data from adequate, well-performed, experimental studies were used to assign hazard designations in preference to those lacking sufficient experimental detail. When multiple adequate studies were available for a given endpoint, any discrepancies that were identified within the set of data were examined further and addressed using a weight-of-evidence approach that was described in the data entry to characterize the endpoint whenever possible.

When available, experimental data from guideline or well-performed experimental studies were preferred (Items 1 and 2 in the hierarchy list). Information from secondary sources such as Material Safety Data Sheets or online databases (such as the National Library of Medicine's Hazardous Substances Data Bank, Item 3 in the hierarchy list) was considered appropriate for some endpoints when it included numerical values for effect levels that could be compared to the evaluation criteria.

4.2.3 Assessment of Polymers

The methodology and procedures used to assess the polymer (butadiene styrene brominated copolymer) in this assessment were slightly different than those used for discrete compounds and simple mixtures. Using the literature search techniques discussed above in Section 4.2.1 experimental data for the polymer were identified for many, but not all, of the endpoints. Estimations, using professional judgment as presented in the polymer assessment literature, were used in instances where there was an absence of experimental data (Boethling and Nabholz 1997).

Polymers are a mixture of molecules with a distribution of components (e.g., different chain lengths) that depend on the monomers used, their molar ratios, the total number of monomeric units in the polymer chain, and the manufacturing conditions. To account for this variation, the average MW profile (also referred to as the number average molecular weight MW_n) was used in the assessment as the individual chains rarely have the same degree of polymerization and weight yet their physical, chemical, and environmental properties are essentially identical for the purposes of this assessment. The polymer evaluated as an alternative, Butadiene styrene brominated copolymer, typically has an average MWs ranging from 60,000 to 160,000 daltons.

4.3 Importance of Physical and Chemical Properties, Environmental Transport, and Biodegradation

Physical-chemical properties provide basic information on the characteristics of a chemical substance and were used throughout the alternatives assessment process. These endpoints provide information required to assess potential environmental release, exposure, and partitioning as well as insight into the potential for adverse toxicological effects. The physical-chemical properties are provided in the individual chemical hazard profiles presented in Section 4.8. For information on how key physical-chemical properties of alternatives can be used to address the potential for human and environmental exposure, please refer to Table 4-1. Descriptions of relevant physical-chemical properties and how they contribute to the hazard assessments are presented below.

Molecular Weight (MW)

MW informs how a chemical behaves in a physical or biological system including bioavailability and environmental fate. In general, but not strictly, larger compounds tend to be less mobile in biological and environmental systems. Their large size restricts their transport through biological membranes and lowers their vapor pressure. Polymers are mixtures that contain a distribution of components and typically do not have a unique MW (see also Section 4.2.3). To account for variation in these mixtures, the average MW or MW_n, determined experimentally (typically using high pressure liquid chromatography, viscosity, or light-scattering), is used in the assessment of the polymer. The assessment of a polymer also includes analysis of oligomers and unchanged monomers (starting materials) that have MW of <1,000 daltons as these can often be the highest concern materials (bioavailable substances) in the mixture. The butadiene styrene

brominated copolymer evaluated in this assessment is not expected to contain a significant amount of oligomers or unchanged monomers based on its method of manufacture.

Melting Point and Boiling Point

These two properties provide an indication of the physical state of the material at ambient temperature. Chemicals with a melting point more than 25°C were assessed as a solid. Those substances with a melting point less than 25°C and a boiling point more than 25°C were assessed as a liquid and those with a boiling point less than 25°C were assessed as a gas. The physical state was used throughout the assessment, such as in the determination of potential routes of human and environmental exposure, as described in Section 5.2. The melting and boiling points were also useful in determining the potential environmental fate, ecotoxicity, and human health hazards of a chemical. For example, organic compounds with high melting points generally have low water solubility and low rates of dissolution. These properties influence a material's bioavailability and were therefore taken into account in both the assessment process and the evaluation of experimental studies. Similarly, chemicals with a low melting point also have a higher potential to be absorbed through the skin, gastrointestinal tract, and lungs.

In the absence of experimental data, the melting point value was not reported and no estimations were performed. If a chemical decomposes before it melts, this information was included in the assessment. For boiling point, the maximum value reported in the assessment was 300°C for high boiling materials including the butadiene styrene brominated copolymer (U.S. EPA 1999b). A melting point for the butadiene styrene brominated copolymer was not reported as this type of material typically reaches a softening point and does not undergo the phase change associated with melting (i.e., solid to liquid).

Vapor Pressure

Vapor pressure is useful in determining the potential for a chemical substance to volatilize to the atmosphere from dry surfaces, from storage containers, or during mixing, transfer, or loading/unloading operations (see Section 5.2). In the assessment process, chemicals with a vapor pressure less than $1x10^{-6}$ mm Hg have a low potential for inhalation exposure resulting from gases or vapors. Vapor pressure is also useful for determining the potential environmental fate of a substance. Substances with a vapor pressure more than $1x10^{-4}$ mm Hg generally exist in the gas phase in the atmosphere. Substances with a vapor pressure between $1x10^{-4}$ and $1x10^{-8}$ mm Hg exist as a gas/particulate mixture. Substances with a vapor pressure less than $1x10^{-8}$ mm Hg exist as a particulate. The potential atmospheric degradation processes described below in the reactivity section generally occur when a chemical exists in the gas phase. Gases in the atmosphere also have the potential to travel long distances from their original point of release. Materials in the liquid or solid (particulate) phases in the atmosphere generally undergo deposition onto the Earth's surface.

A maximum vapor pressure of $1x10^{-8}$ mm Hg was assigned for chemicals without experimental data or for those substances that were anticipated by professional judgment to be nonvolatile (U.S. EPA 1999b). The maximum vapor pressure of $1x10^{-8}$ mm Hg was also the default value

reported for the vapor pressure of the butadiene styrene brominated copolymer as it has a MW >1,000 daltons.

Water Solubility

The water solubility of a chemical provides an indication of its distribution between environmental media, potential for environmental exposure through release to aquatic compartments, and potential for human exposure through ingestion of drinking water. Water solubility was also used extensively to determine potential human health and ecotoxicity hazards. In general, chemicals with water solubility less than $1x10^{-5}$ g/L indicate a lower concern for both the expression of adverse effects, and potential aquatic and general population exposure due to their low bioavailability. However, chemicals with low bioavailability also tend to be more environmentally persistent. Low bioavailability is different than no bioavailability, and the two should not be used interchangeably.

Within the context of this alternatives assessment, the following descriptors were used according to ranges of water solubility values: more than 10,000 mg/L was considered very soluble; 1,000–10,000 mg/L represents soluble; 100–1,000 mg/L represents moderately soluble, 1–100 mg/L represents slightly soluble, and less than 1 mg/L represents insoluble, noting that these guidelines might not match what is used elsewhere within the scientific literature for other disciplines. Chemicals with higher water solubility were more likely to be transported into groundwater with runoff during storm events, be absorbed through the gastrointestinal tract or lungs, partition to aquatic compartments, undergo atmospheric removal by rain washout, and possess a greater potential for human exposure through the ingestion of contaminated drinking water. Chemicals with lower water solubility are generally more persistent and have a greater potential to bioconcentrate.

The water solubility of a substance was also used to evaluate the quality of experimental aquatic toxicity and oral exposure human health studies as well as the reliability of aquatic toxicity estimates. If the water solubility of a substance was lower than the reported exposure level in these experiments, then the study was likely to be regarded as inadequate due to potentially confounding factors arising from the presence of un-dissolved material. For aquatic toxicity estimates obtained using SARs, when the estimated toxicity was higher than a chemical's water solubility (i.e., the estimated concentration in water at which adverse effects appear cannot be reached because it was above the material's water solubility), the chemical was described as having NES. An NES designation is equivalent to a Low ecotoxicity hazard designation for that endpoint.

Chemicals without experimental data or chemicals that were anticipated by professional judgment to be sufficiently insoluble and thus were not bioavailable were assigned a water solubility maximum value of $1x10^{-3}$ mg/L (U.S. EPA 1999b). A water solubility of $1x10^{-3}$ mg/L is the default value used for discrete organics as well as a non-ionic polymer with a MW >1,000 daltons according to information contained in the literature concerning polymer assessment (Boethling and Nabholz 1997). This assignment is consistent with an analysis of the chemicals used in the development of the water solubility estimation program in EPA's EPISuite™ software. The training set for this model included 1,450 chemicals with a MW range 27-628

daltons and experimental water solubilities ranging from miscible to $4x10^{-7}$ mg/L (Meylan, Howard et al. 1996; U.S. EPA 2011h). Given that water solubility decreases with MW, a default value of $1x10^{-3}$ mg/L is consistent with the limited bioavailability expected for materials with a MW >1,000 daltons.

Octanol/Water Partition Coefficient (K_{ow})

The octanol/water partition coefficient, commonly expressed as its log value (i.e., log K_{ow}) is one of the most useful properties for performing a hazard assessment. The log K_{ow} indicates the partitioning of a chemical between octanol and water, where octanol is used to mimic fat and other hydrophobic components of biological systems. Chemicals with a log K_{ow} less than 1 are highly soluble in water (hydrophilic), while those with a log K_{ow} more than 4 are not very soluble in water (hydrophobic). A log K_{ow} more than 8 indicates that the chemical is not readily bioavailable and is essentially insoluble in water. In addition, a log K_{ow} greater than approximately 8 may be difficult to obtain experimentally.

The log K_{ow} can be used as a surrogate for the water solubility in a hazard assessment and is frequently used to estimate the water solubility if an experimental value is not available. It can also be used to estimate other properties important to the assessment, including bioconcentration and soil adsorption, and is a required input for SAR models used to estimate ecotoxicity values.

For chemicals without data, that are not within the domain of EPISuite™ or that were expected to be insoluble in water (WS $<1x10^{-3}$ mg/L), a minimum value of 10 was assigned for the log K_{ow} (U.S. EPA 1999b). Insoluble chemicals that could be run through EPISuite™ software may use a log K_{ow} >10 if the result appeared to be valid based on expert review. This assignment is consistent with an analysis of the chemicals ("training set") used in the development of the octanol/water partition coefficient estimation program in the EPISuite™ software. The training set for this model included 10,946 chemicals with a MW range 18-720 daltons and experimental log K_{ow}s ranging from -3.89 to 8.70 (Meylan and Howard 1995; U.S. EPA 2011g). Given that log K_{ow} increases with MW, a default value of 10 is consistent with the limited bioavailability expected for materials with a MW >1,000 daltons. A maximum log K_{ow} of -2 was used for water soluble materials. For most polymers and other materials that are anticipated to be insoluble in both water and octanol, the log K_{ow} cannot be measured and it was therefore not listed for the butadiene styrene brominated copolymer evaluated in this assessment.

Flammability (Flash Point)

The flash point of a substance is defined as the minimum temperature at which the substance emits sufficient vapor to form an ignitable mixture with air. Flash point can be used to identify hazards associated with the handling of volatile chemicals. Substances with a flash point above 37.8°C (100°F) were commonly referred to as non-flammable, as this is the flammability definition used in the shipping industry. There are exceptions to this definition such as chemicals that may form explosive mixtures in the presence of air.

Explosivity

Explosivity refers to the potential for a chemical to form explosive mixtures in air and can be defined using the limits of flammability. The lower limit of flammability (LFL) is defined as the minimum concentration of a combustible substance that is capable of propagating a flame through a homogenous mixture in the presence of an ignition source. The upper limit of flammability (UFL) is similarly defined as the highest concentration that can propagate a flame. LFLs and UFLs are commonly reported as the volume percent or volume fraction of the flammable component in air at 25°C. If the ambient air concentration of the gas (or vapor) is between the upper and lower explosion limit, then the material has the potential to explode if it comes in contact with an ignition source. Knowledge regarding the explosivity of a given material in air is also useful in identifying potential hazards associated with the manufacture and use of that material.

pH

The pH scale measures how acidic or basic a substance is on a range from 0 to 14. A pH of 7 is neutral. A pH less than 7 is acidic, and a pH greater than 7 is basic. This scale is used primarily to identify potential hazards associated with skin or eye contact with a chemical or its aqueous solutions. The corrosive nature of chemicals that form either strongly basic (high pH) or strongly acidic (low pH) solutions are generally likely to result in harm to skin and other biological membranes. For corrosive chemicals, some experimental studies, such as biodegradation tests, require additional analysis to determine if the tests were performed at concentrations that cause harm to microbes in the test (and, therefore, may result in incorrectly identifying a chemical as persistent in the environment). For chemicals that form moderately basic or acidic solutions in water, the pH of the resulting solution can be used in lieu of a measured dissociation constant. None of the chemicals evaluated in this assessment are expected to dissociate in water.

Dissociation Constant in Water (pK_A)

The dissociation constant determines if a chemical will ionize under environmental conditions. The dissociation constant in water provides the amount of the dissociated and undissociated forms of an acid, base, or organic salt in water. Knowledge of the dissociation constant is required to assess the importance of the other physical-chemical properties used in the hazard assessment. As the percentage of ionization increases, the water solubility increases while the vapor pressure, Henry's Law constant, and octanol/water partition coefficient decrease. For acids and bases, the dissociation constant is expressed as the pK_A and pK_B, respectively. None of the chemicals evaluated in this assessment are expected to ionize in water.

Henry's Law Constant

Henry's Law constant is the ratio of a chemical's concentration in the gas phase to that in the liquid phase (at equilibrium). In environmental assessments, the Henry's Law constant is typically measured in water at 25°C. The Henry's Law constant provides an indication of a chemical's volatility from water, which can be used to derive partitioning within environmental compartments and the amount of material removed by stripping in a sewage treatment plant.

Henry's Law constant values less than $1x10^{-7}$ atm-m^3/mole indicate slow volatilization from water to air (the Henry's Law constant for the volatilization of water from water is $1x10^{-7}$ atm-m^3/mole) and values more than $1x10^{-3}$ atm-m^3/mole indicate rapid volatilization from water to air. To aid in determining the importance of volatilization, the assessment uses two models based on the Henry's Law constant. These models determine the half-life for volatilization from a model river and a model lake. A maximum value of $1x10^{-8}$ atm-m^3/mole for the Henry's Law constant was assigned for chemicals without experimental data or for those that were anticipated by professional judgment to be nonvolatile.

Sediment/Soil Adsorption/Desorption Coefficient (K_{oc})

The soil adsorption coefficient provides a measure of a chemical's ability to adsorb to the organic portion of soil and sediment. This provides an indication of the potential for the chemical to leach through soil and be introduced into groundwater, which may lead to environmental exposures to wildlife or humans through the ingestion of drinking water drawn from underground sources. Chemicals with high soil adsorption coefficients are expected to be strongly adsorbed to soil and are unlikely to leach into ground water. The soil adsorption coefficient also describes the potential for a chemical to partition from environmental waters to suspended solids and sediment. The higher the K_{oc}, the more strongly a chemical is adsorbed to soil. Strong adsorption may impact other fate processes, such as the rate of biodegradation, by making the chemical less bioavailable.

The soil adsorption coefficient, K_{oc}, is normalized with respect to the organic carbon content of the soil to account for geographic differences. The assignments for the degree that a chemical is adsorbed to soil within the context of the assessment were described qualitatively as very strong (above 30,000), strong (above 3,000), moderate (above 300), low (above 30), and negligible (above 3). When determining the potential for a chemical to adsorb to soil and suspended organic matter, the potential for a chemical to form chemical bonds with humic acids and attach to soil also needs to be considered, although this process is generally limited to a small number of chemical classes.

A maximum value of 30,000 for the K_{oc} was assigned for chemicals without experimental data or for those that were anticipated by estimation models or professional judgment to be strongly absorbed to soil (U.S. EPA 2005b). A default K_{oc} of 30,000 was also assigned for the butadiene styrene brominated copolymer because it has a MW >1,000 daltons.

Reactivity

The potential for a substance to undergo irreversible chemical reactions in the environment can be used in the assessment of persistence. The primary chemical reactions considered in an environmental fate assessment are: hydrolysis, photolysis, and the gas phase reaction with hydroxyl radicals, ozone, or nitrate radicals. The most important reaction considered in the hazard assessment of organic compounds is hydrolysis, or the reaction of a chemical substance with water. Because the rate of hydrolysis reactions can change substantially as a function of pH, studies performed in the pH range typically found in the environment (pH 5–9) were considered. The second reaction considered in the assessment is photolysis, the reaction of a chemical with

sunlight. Both hydrolysis and photolysis occur in air, water, and soil, while only hydrolysis was considered in sediment. The half-lives for reactive processes, if faster than removal via biodegradation, were used to assign the hazard designation by direct comparison to the DfE persistence criteria.

For the atmospheric compartment, persistence also includes the evaluation of oxidative gas-phase processes. These processes include the reaction with ozone, hydroxyl radicals, and nitrate radicals. Since the average concentration of these oxidative species in the atmosphere has been measured, the experimental or estimated rate constants were converted to, and reported as, a half-life in the assessment using standard pseudo first-order kinetics (U.S. EPA 2011e; U.S. EPA 2011d).

Environmental Transport

The persistence of a chemical substance is based on determining the importance of removal processes that may occur once a chemical enters the environment. As noted in Section 4.3, chemicals with a half-life of less than 60 days are expected to be at most a Moderate hazard designation for persistence. Persistence does not directly address the pathways in which a chemical substance might enter the environment (e.g., volatilization or disposal in a landfill) and focuses instead on the removal processes that are expected to occur once it is released into air, water, soil, or sediment. Similarly, the persistence assessment does not address what might happen to a chemical substance throughout its life cycle, such as disposal during incineration of consumer or commercial products. Understanding the environmental transport of a chemical substance can help identify processes relevant to environmental assessment. For example, if a chemical is toxic to benthic organisms and partitions primarily to sediment, its potential release to water should be carefully considered in the selection of alternatives.

Biodegradation

In the absence of rapid hydrolysis or other chemical reactions, biodegradation is typically the primary environmental degradation process for organic compounds. Determining the importance of biodegradation is, therefore, an important component of the assessment. Biodegradation processes are divided into two types. The first is primary biodegradation, in which a chemical substance is converted to another substance. The second is ultimate biodegradation, in which a chemical is completely mineralized to small building-block components (e.g., CO_2 and water). DfE persistence criteria use data that are reported as percent of theoretical ultimate degradation in the guideline Ready Biodegradability test or as a half-life in other experimental studies; both of these measurements can be compared directly to the DfE criteria in 4.1.2. When considering primary degradation, the assessment process includes an evaluation of the potential for the formation of metabolites that were more persistent than the parent materials. Chemical substances that undergo rapid primary degradation but only slow ultimate biodegradation were considered to have stable metabolites. In the absence of measured data on the substance of interest, DfE evaluated the potential for biodegradation for chemicals with a MW <1,000 daltons using the EPA EPISuite™ models. EPISuite™ estimates the probability for ready biodegradation as well as the potential for primary and ultimate removal, as described in Section 4.3. A default Very High persistence hazard designation was assigned for the butadiene styrene brominated

copolymer according to information contained in the literature concerning polymer assessment because it has a MW >1,000 daltons (Boethling and Nabholz 1997).

4.4 Evaluating Human Health Endpoints

After data collection and analysis of the physical-chemical properties for the chemicals being assessed the comparison of the data against the hazard criteria can begin. Section 4.4.1 discusses how measured data are used to make hazard designations for human health endpoints and Section 4.4.2 presents the approach for filling in data gaps to make these hazard designations.

4.4.1 Endpoints Characterized and Evaluated Against Criteria Based on Measured Data

This section provides a short description of how measured data were used to designate the level of hazard for each endpoint. As a reminder, the criteria for the hazard designations are in Table 4-2.

For acute mammalian toxicity, LD_{50}s or LC_{50}s were used to assign the hazard designation. Four levels of hazard designation have been defined ranging from Low to Very High.

For cancer, the hazard designation was contingent on the level of evidence for increased incidence of cancer rather than potency. The definitions applied in DfE criteria are based on International Agency for Research on Cancer (IARC) levels of evidence (International Agency for Research on Cancer 2006). For example, a designation of Very High concern requires that the substance be characterized as a "known or presumed human carcinogen", whereas a designation of Low concern requires either negative studies or robust SAR conclusions. A designation of Moderate was applied as a default value when there was an absence of data suggesting High carcinogenicity, and an absence of data supporting Low carcinogenicity (i.e., a lack of negative studies or weak SAR conclusions).

Similarly, the hazard designation for mutagenicity/genotoxicity was also based on the level of evidence rather than potency. Complete data requirements for this endpoint were both gene mutation and chromosomal aberration assays. For instances of incomplete or inadequate mutagenicity/genotoxicity data, a Low hazard designation cannot be given.

For chronic endpoints, such as reproductive, developmental, neurological, and repeated dose toxicities, the hazard designation was based on potency. The evaluation considers both lowest observed adverse effect levels (LOAELs) and identification of no observed adverse effect levels (NOAELs) when available. The LOAEL and the NOAEL are experimental dose levels, and their reliability is dictated by the study design. In studies for which the lowest dose tested resulted in an adverse effect (and therefore a NOAEL was not established), and in studies for which the highest dose tested was a NOAEL, a conservative approach using professional judgment was used to address uncertainty regarding the lowest dose or exposure level that might be expected to cause a particular adverse effect. For example, in the absence of an established a NOAEL, an identified LOAEL might fall within the range of a Moderate hazard; however, it is uncertain if a lower dose, such as one that falls within the range of High hazard exists because no lower doses were tested. In such cases, professional judgment was applied to assign a hazard designation when possible. Some degree of uncertainty was evident in results from studies in which a

NOAEL may fall within one hazard range (e.g., Moderate hazard) and the identified LOAEL falls within a different hazard range (e.g., Low hazard) because the true LOAEL may fall in either category, but there were not enough experimental data points to determine the true LOAEL. Professional judgment was also applied to these cases to assign a hazard descriptor when possible and the rationale used was described in the assessment. Developmental neurotoxicity was considered and was evaluated using the developmental toxicity criteria, which are more stringent than the criteria for neurotoxicity, and thus designed to be more protective (U.S. EPA 2011b).

The criteria for skin and respiratory sensitization, which are immune-based responses, consider the frequency and potency of the reactions. For skin sensitization, categories were based on the weight of evidence[15] from traditional animal bioassays, but *in vitro* alternative studies were also considered. At this time, there are no standard test methods for respiratory sensitization and no test data; as a result there was often no designation for this endpoint.

The evaluation of skin and eye irritation and corrosivity were based on the time to recovery.

4.4.2 SAR – Application of SAR and Expert Judgment to Endpoint Criteria

If measured data pertaining to human health criteria were not available, potential adverse effects were estimated with SAR analysis. To make these estimates, DfE relied on the expertise of scientists in EPA's New Chemicals Program who have reviewed thousands of chemicals and associated data using these methods. SAR uses the molecular structure of a chemical to infer a physicochemical property that can be related to specific effects on human health. These correlations may be qualitative ("simple SAR") or quantitative (QSAR). Information on EPA's use of SAR analysis has been published by U.S. EPA (1994). Public access to free validated quantitative SAR models for human health endpoints is far more limited than physical-chemical properties, environmental fate parameters, or ecotoxicology.

Carcinogenicity was assessed using the OncoLogic expert system that provides a qualitative result directly applicable to the DfE criteria. For other endpoints that required SAR approaches, an analog approach using expert judgment was used as discussed in Section 4.4.2. All estimates obtained in this project were reviewed by EPA scientists having appropriate expertise. Estimates for the other human health endpoints were based on expert judgment using an analog approach and not through the use of computerized SAR methodologies.

Carcinogenicity

The potential for a chemical to cause cancer in humans was estimated using the OncoLogic expert system. This program uses a decision tree based on the known carcinogenicity of chemicals with similar chemical structures, information on mechanisms of action, short-term predictive tests, epidemiological studies, and expert judgment. EPA's OncoLogic expert system

[15] Generally, weight of evidence is defined as the process for characterizing the extent to which the available data support a hypothesis that an agent causes a particular effect (U.S. EPA 1999a; U.S. EPA 2002; U.S. EPA 2005a).

was consulted, but did not provide results for HBCD or the alternatives because an appropriate chemical class was not available for HBCD or the alternatives.

Assessment of Polymers

Estimates for the butadiene styrene brominated copolymer were obtained using information contained in the literature concerning polymer assessment based on its MW profile (Boethling and Nabholz 1997). The butadiene styrene brominated copolymer had an average MW >1,000 daltons and no significant amounts of low MW material <1,000 daltons arising from oligomers or unreacted monomers based on its method of manufacture. The properties for polymers with an average MW >1,000 with no low MW components are generally evaluated as a single high MW material. In general, polymers with an average MW >1,000 were not amenable to the available SAR estimation methods and based on the literature are assumed to have low to no bioavailability. Polymers with MW >1,000 that were not degradable or reactive are also typically not bioavailable. Polymers with an average MW >10,000 have the potential for adverse effects due to lung overloading when respirable particles are present (less than ten microns). The potential for fibrosis or cancer are not assumed with high MW compounds. These methods were applied to the butadiene styrene brominated copolymer evaluated in this hazard screening assessment. There may be exceptions to the guidelines outlined above and as such this guidance should not be held as absolute thresholds.

4.5 Evaluating Environmental Toxicity and Fate Endpoints

As with endpoints previously mentioned, the preferred method for the evaluation of environmental endpoints is the use of experimental data. In their absence, the alternatives assessment uses computerized QSAR models developed by EPA for the evaluation of environmental endpoints that can be directly compared to the DfE criteria. When measured data were not available, the aquatic toxicity was estimated using EPA's ECOSAR™ software and the persistence designation was estimated using models in EPA's EPISuite™ software. The hazard designation was determined by applying the criteria to these estimates. As a direct result of the design of these models and their direct application to DfE criteria, the evaluation of environmental endpoints using experimental or estimated data was discussed together in the following subsections.

4.5.1 Aquatic Toxicity

For ecological toxicity, the alternatives assessment focused on the hazard designations for acute and chronic studies on freshwater species of algae, invertebrates, and fish, (often referred to as the "three surrogate species"). Aquatic toxicity values were reported in the assessment as follows:

- Acute (estimated or experimental) - LC_{50} in mg/L
- Chronic (experimental) - No observed effect concentration (NOEC) in mg/L
- Chronic (estimated) - ChV, or the geometric mean between the NOEC and the LOEC, in mg/L

Experimental data reported in the alternatives assessment also included information on the species tested. Test data on other organisms (e.g., worms) were included in the assessment if data were readily available. These data would be evaluated using professional judgment to support hazard designations assigned using the three surrogate species; however, they were not used by themselves to assign a hazard designation as DfE criteria are not available.

If an experimental or estimated effect level exceeded the known water solubility of a chemical substance, or if the log K_{ow} exceeded the estimated ECOSAR™ cut-off values for acute and chronic endpoints (which are class-specific), NES were predicted for the aquatic toxicity endpoints. NES indicates that at the highest concentration achievable, the limit of a chemical's water solubility, no adverse effects were observed (or would be expected). In these cases, a Low hazard designation was assigned. The three alternatives evaluated were estimated to display NES.

In the case where an experimental aquatic toxicity value was significantly higher than the chemical's water solubility, it was likely the result of a poorly conducted study. In this circumstance, which is generally more frequent for formulated products or mixtures, additional details were provided in the data quality section to describe why the reported values could not be used to assign a hazard designation.

EPA's ECOSAR™ estimation program uses chemical structure to estimate toxicity of a chemical substance using class-specific QSARs. ECOSAR™ automatically determines all of the classes that a chemical substance may belong to and, therefore, may provide a number of different ecotoxicity estimates for some or all of the species and durations estimated. Modeled results are dependent on the functional groups present on the molecule as well as the diversity of chemicals with experimental data that were used to build the models (their training set). The hazard profiles report every estimated value returned from ECOSAR™. However, the hazard designation was based on the most conservative ECOSAR™ estimate, unless expert judgment suggested that an individual substance was better represented by a specific class based on analysis of the operative mode of action. However, if the chemical substance is not anticipated to lie within the domain of the class-specific estimates provided by ECOSAR or to undergo the same mode of action of the chemicals that appear in their training sets, the narcosis (baseline toxicity) associated with the neutral organic class will be used preferentially. Experimental log K_{ow} values were used preferentially as input into ECOSAR™. In their absence, estimated log K_{ow} values from EPISuite™ were used. ECOSAR™ is maintained and developed as a stand-alone program but is also accessible through the EPA EPISuite™ program after it is installed; therefore the Estimations Program Interface (EPI) program was cited for the ECOSAR™ values in this report.

The QSARs for ECOSAR™ were built using experimental data for several chemical classes. For a chemical class to be defined within ECOSAR™, sufficient acute experimental data were required to build a QSAR for all three species included in the model. The equations in ECOSAR are derived from data for surrogate species of fish, zooplankton, and phytoplankton. While these surrogate species can comprise several genera as well as families, the equations are not intended to be species specific, but rather estimates of toxicity to the general trophic levels they represent (fish, aquatic invertebrates, and aquatic plants). There were instances, however, where sufficient experimental data are not available to build a chronic QSAR for some of the three surrogate

species. Although not utilized in this alternative assessment an acute value (experimental or estimated) would be divided by an acute to chronic ratio (ACR) to arrive at the chronic value if a chronic equation did not exist. ACRs of 10 are used for fish and daphnid and an ACR of 4 is used for algae (Mayo-Bean, Nabholz et al. 2011).

An estimate of NES is the default value used for organics, oligomers, or non-ionic polymers with a MW >1,000 daltons in the assignment of aquatic toxicity hazard. In EPA's New Chemical program, aquatic toxicity is not predicted for chemicals with a MW >1,000 daltons as uptake has been found to decrease exponentially with MWs >600 daltons (Nabholz, Clements et al. 1993) due to a decrease in passive absorption through respiratory membranes (Mayo-Bean, Nabholz et al. 2011).

4.5.2 Bioaccumulation

Bioaccumulation is a process in which a chemical substance is absorbed in an organism by all routes of exposure as occurs in the natural environment, e.g., from dietary and ambient environment sources. Bioaccumulation is the net result of the competing processes which includes uptake, metabolism, and elimination of a chemical in an organism. Bioaccumulation can be evaluated using the BAF, the steady state ratio of a chemical in an organism relative to its concentration in the ambient environment, where the organism is exposed through ingestion and direct contact. Experimental BAFs have not been widely available in the scientific literature and, as a result, experimental BCFs are more commonly used to evaluate the bioaccumulation hazard. BCFs are defined as the ratio of the concentration of a chemical in an organism to the concentration of the chemical in the organism's surroundings; BCFs are typically measured for fish (in water) using guideline studies.

Experimental BAF or BCF values can be compared directly to the DfE criteria for this endpoint to assign a hazard designation. The BCF/BAF designations range from <100 for a Low designation to >5,000 for a Very High designation (see 4.1.2). If experimental values were available for both of these endpoints, and the BCF and BAF were >100 (i.e., above the Low designation), the largest factor was used to assign hazard designation. If experimental BCFs <100 were available, the estimated upper trophic BAF from EPISuite™ was used preferentially if its use resulted in a more conservative hazard designation and the potential for metabolism was accurately accounted for within the model estimates.

In the absence of experimental data, evaluation of bioaccumulation potential can be done using the log K_{ow} and the log octanol/air partition coefficient, K_{oa}, as estimated by EPISuite™. However, analysis using K_{oa} requires the use of metabolism data for higher trophic, air-breathing organisms, which can be difficult to obtain from the scientific literature and cannot be readily estimated. BAFs and BCFs from EPISuite™ were, therefore, typically used for the bioaccumulation hazard designation when experimental data were lacking. These values can be compared directly to DfE criteria and the most conservative result was used for the hazard designation. For chemicals that had estimated bioaccumulation data, available experimental monitoring data were used to provide insight into the reliability of the model results. For example, an estimated Low bioaccumulation potential may be increased to a Moderate designation if a chemical was routinely identified in samples from higher trophic levels, or a High designation if the chemical was routinely measured in animals at the top of the food chain.

Environmental monitoring data were only available for HBCD and TBBPA bis(2,3-dibromopropyl) ether.

An estimate of Low is the default value used for discrete organics with a MW >1,000 daltons in the assignment of bioaccumulation hazard. This assignment is consistent with an analysis of the chemicals used in the development of the bioconcentration and bioaccumulation estimation programs in the EPISuite™ software (U.S. EPA 2011f). The training sets for these models included 527 and 421 chemicals, respectively, with a MW range of 68-992 daltons (959 daltons for BAF). Given that BCF and BAF reach a maximum and then decrease with increasing log K_{ow}, a default value of Low is, in general, consistent with the limited bioavailability expected for materials with a MW >1,000 daltons. DfE will use all available well-conducted studies when evaluating bioaccumulation potential for materials with a MW >1,000, including environmental biomonitoring data on higher trophic levels. No discrete organic substances with a MW >1,000 daltons were evaluated in the HBCD alternatives assessment.

The butadiene styrene brominated copolymer has a MW >1,000 daltons, and the default bioaccumulation designation of Low was assigned, arising from its predicted limited bioavailability (Boethling and Nabholz 1997).

4.5.3 Environmental Persistence

A chemical's persistence in the environment is evaluated by determining the type and rate of potential removal processes. These removal processes were generally divided into two categories: chemical and biological. Of the chemical degradation processes, an evaluation of environmental persistence includes the reaction of a chemical with water, also known as hydrolysis, because water is ubiquitous in the environment. Hydrolysis rate constants can be obtained from the literature or estimated, and the resulting half-lives can be compared directly to DfE criteria. For chemicals without hydrolyzable groups, biodegradation tends to be the faster degradation process; however, numerous chemicals possess labile groups and these may hydrolyze in the environment at significant or even rapid rates. The chemicals assessed are not anticipated to hydrolyze under environmental conditions. Direct and indirect photolysis also represent other potential chemical degradation processes that are considered in the alternative assessment, and they are discussed later in this section.

Biodegradation, the most prevalent biological removal process, was divided into two types. The first is primary biodegradation, in which a chemical substance is converted to another substance through a single transformation. The second is ultimate biodegradation, in which a chemical is completely degraded to CO_2, water, mineral oxides (such as phosphates for chemicals containing phosphorus). DfE criteria utilize ultimate biodegradation preferentially for the persistence hazard designation, although primary removal rates were informative in assigning hazard designations particularly for materials that were transformed slowly, and to a lesser extent for those that are transformed rapidly.

If ultimate biodegradation data were not available, primary removal data were evaluated. If primary removal processes are occurring, then the potential for the formation of degradation products that are more persistent than the parent compounds must be considered in the hazard designation. When present, the persistent degradation products should be evaluated for fate and

toxicity if they are anticipated to result in a different hazard designation relative to the parent material. For all four of the chemicals evaluated, the primary biodegradation step is anticipated to occur at a slow or negligible rate representing a High or Very High designation when compared directly to the DfE criteria.

Biodegradation processes can be classified as either aerobic or anaerobic. Aerobic biodegradation is an oxidative process that occurs in the presence of oxygen. Anaerobic biodegradation is a reductive process that occurs only in the absence of oxygen. Aerobic biodegradation is typically assessed for soil and water, while anaerobic biodegradation is generally assessed in sediment. For determining the persistence hazard, the importance of both aerobic and anaerobic biodegradation as well as partitioning and transport in the environment were considered to determine what removal processes were most likely to occur. Anaerobic degradation may use any of several electron acceptors depending on their availability in a given environment and the prevailing redox potential (E_h). The biodegradative populations that are dominant in a given environment vary with the conditions and so do their biodegradative capabilities.

One aspect of the assessment is to determine the potential for removal of a chemical substance, and especially removal attributable to biodegradation, within a sewage treatment plant and other environments. In this assessment, the term "ready biodegradability" refers to a chemical's potential to undergo ultimate degradation in guideline laboratory studies. A positive result in a test for ready biodegradability can be considered as indicative of rapid and ultimate degradation in most environments including biological sewage treatment plants. Ready tests typically include a 10-day window, beginning when the biodegradation parameter (e.g., disappearance of dissolved organic carbon from test substance, or theoretical oxygen demand) reaches 10%. The 10-day window must occur within the 28-day length of the test. If the pass level of the test (60% for oxygen demand and CO_2 production; 70% for dissolved organic carbon disappearance) is met in the 10-day window, the chemical received a Very Low hazard designation. Those that did not pass the 10-day window criterion but met the pass level in 28 days received a Low hazard designation.

In the absence of a reported half-life, experimental data were also used to approximate half-life as appropriate. For example, a chemical that undergoes <5% removal in 30 days would be expected to have a half-life >60 days and would be assigned a High persistence concern.

When experimental data on the biodegradation of a chemical substance were not available, the potential of that substance to undergo this removal process was assessed from the results of the EPISuite™ models. These models fall into one of four classes: rapid biodegradation models based on linear and non-linear regressions that estimate the probability that a chemical substance will degrade fast; expert survey models that estimated the rate of ultimate and primary biodegradation using semi-quantitative methods; probability of ready biodegradability in the OECD 301C test; and probability of rapid biodegradation under methanogenic anaerobic conditions (specifically, under conditions of the OECD 311 test). Each of these is discussed in the following paragraphs.

The first models (Biowin 5 and 6) used in the screening assessment estimated ready biodegradability in the OECD 301C test and are also known as the Japanese Ministry of International Trade and Industry (MITI) models. These models provided the probability that a material passes this standardized test. Those chemicals that were estimated to pass the ready biodegradability test received a Low persistence designation. If a chemical was not estimated to pass the MITI test, the results of the other EPISuite™ biodegradation models were used.

The rapid biodegradation potential models within EPISuite™ (Biowin 1 and 2) were useful for determining if a chemical substance was expected to biodegrade quickly in the environment. If a chemical was likely to biodegrade quickly, it was generally assigned a Low hazard designation for persistence. The results of the estimates from these models may be used in concert with the semi-quantitative output from a second set of models, which include ultimate and primary biodegradation survey models (Biowin 3 and 4) for evaluating persistence. These models provided a numeric result, ranging from 1 to 5, which relates to the amount of time required for complete ultimate degradation (Biowin 3) and removal of the parent substance by primary degradation (Biowin 4) of the test compound. The numeric result from Biowin 3 was converted to an estimated half-life for removal that can be compared directly to DfE criteria. If results from different models (other than the MITI models) led to a different hazard designation, then the ultimate biodegradation model results were used preferentially. If the transport properties indicate the potential for the material to partition to sediment, an anoxic compartment, then the results of the anaerobic probability model (Biowin 7) will also be evaluated.

Half-lives for hydrolysis from experimental studies or EPISuite™ estimates were used in preference to biodegradation data when they suggested that hydrolysis is a more rapid removal process. Hydrolysis half-lives can then be compared directly to DfE criteria to assign the persistence designation. None of the chemicals evaluated are anticipated to undergo hydrolysis under environmental conditions.

Photolysis may also be an important environmental removal process. In general, environmental removal rates from photolysis do not compete with biodegradation or hydrolysis although there are exceptions such as iodides and, to a lesser extent, bromides. Photolysis may be an important removal process for chemicals that were not bioavailable because of their limited water solubility. Estimation methods for photolysis rates were not available using computerized SAR tools. If experimental or suitable analog data were available, the rate of photolysis was evaluated relative to other removal processes.

The environmental persistence designation in the four hazard profiles is High or Very High. Although these substances can degrade over time, this process is anticipated to occur at a very slow rate. The butadiene styrene brominated copolymer has a MW >1,000 and received a Very High persistence designation arising from its lack of bioavailability and the absence of chemical degradation processes.

4.6 Endocrine Activity

Chemicals included in DfE alternatives assessments were screened for potential endocrine activity, consistent with the DfE Alternatives Assessment Criteria. **Endocrine activity** refers to a change in endocrine homeostasis caused by a chemical or other stressor. An **endocrine**

disruptor is an external agent that interferes in some way with the role of natural hormones in the body, in a manner causing adverse effects. Relevant data are summarized in the hazard assessments for each chemical, located in Section 4.8. Data on endocrine activity were available for HBCD, tetrabromobisphenol A (TBBPA) bis (2, 3-dibromopropyl) ether, and for TBBPA-bis brominated ether derivative by analogy to the former substance. Endocrine data were summarized as a narrative. A unique hazard designation for endocrine activity is not provided for this endpoint in Table 4-2 because there is no consensus on what constitutes Low, Moderate or High hazard concern. This issue is discussed in greater detail below.

The document *Special Report on Environmental Endocrine Disruption: An Effects Assessment and Analysis* describes EPA's activities regarding the evaluation of endocrine disruption (U.S. EPA 1997). This report was requested by the Science Policy Council and prepared by EPA's Risk Assessment Forum. This report states that "Based on the current state of the science, the Agency does not consider endocrine disruption to be an adverse endpoint per se, but rather to be a mode or mechanism of action potentially leading to other outcomes, for example, carcinogenic, reproductive or developmental effects, routinely considered in reaching regulatory decisions" (U.S. EPA 1997). The report also states that "Evidence of endocrine disruption alone can influence priority setting for further testing and the assessment of results of this testing could lead to regulatory action if adverse effects are shown to occur" (U.S. EPA 1997).

The 1996 Food Quality Protection Act (FQPA) directed EPA to develop a scientifically validated screening program to determine whether certain substances may cause hormonal effects in humans. In response, EPA established the Endocrine Disruptor Screening Program (EDSP) (U.S. EPA 2012b). The EDSP is developing requirements for the screening and testing of thousands of chemicals for their potential to affect the endocrine system. When complete, EPA will use these screening and testing approaches to set priorities and conduct further testing when warranted. The science related to measuring and demonstrating endocrine disruption is relatively new, and validated testing methods at EPA are still being developed.

The EDSP proposes a two-tiered approach that includes initial screening followed by more in-depth testing when warranted (U.S. EPA 2011a). The Tier 1 screening battery is intended to identify chemicals with the potential to interact with the estrogen, androgen, or thyroid hormone systems through any of several recognized modes of action. Positive findings for Tier 1 tests identify the potential for an interaction with endocrine systems, but do not fully characterize the nature of possible effects in whole animals. Tier 2 testing is intended to confirm, characterize, and quantify the effects for chemicals that interact with estrogen, androgen, and thyroid hormone systems. These test methods must undergo a four-stage validation process (protocol development, optimization/prevalidation, validation, and peer-review) prior to regulatory acceptance and implementation. Validation is ongoing for Tier 1 and Tier 2 methods.[16] Once validated test methods have been established for screening and testing of potential endocrine disruptors, guidance must be developed for interpretation of these test results using an overall weight-of-evidence characterization.

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[16] Information on the status of assay development and validation efforts for each assay in EPA's EDSP can be found at: http://www.epa.gov/oscpmont/oscpendo/pubs/assayvalidation/status.htm.

To assess the data on endocrine activity, DfE applies the weight of evidence approach developed by the EDSP (U.S. EPA 2011c). This process integrates and evaluates data, and always relies on professional judgment (U.S. EPA 2011c). To evaluate endocrine activity with this weight of evidence approach, DfE examined multiple lines of evidence (when available) and considered the nature of the effects within and across studies, including number, type, and severity/magnitude of effects, conditions under which effects occurred (e.g., dose, route, duration), consistency, pattern, range, and interrelationships of effects observed within and among studies, species, strains, and sexes, strengths and limitations of the *in vitro* and *in vivo* information, and biological plausibility of the potential for an interaction with the estrogen, androgen, or thyroid hormonal pathways.

Test data from both *in vitro* assays and *in vivo* studies were included in the hazard profile for HBCD. The hazard profile for TBBPA bis(2, 3-dibromopropyl) ether includes summaries of *in vitro* assays, as does the hazard profile for TBBPA-bis brominated ether derivative by analogy to the former substance. The results of *in vitro* assays alone were not generally expected to provide a sufficient basis to support a hazard designation for endocrine disruption. EPA expects that *in vivo* evidence would typically be given greater overall influence in the weight of evidence evaluation than *in vitro* findings because of the inherent limitations of such assays. Although *in vitro* assays can provide insight into the mode of action, they have limited ability to account for normal metabolic activation and clearance of the compound, as well as normal intact physiological conditions (e.g., the ability of an animal to compensate for endocrine alterations). There were no experimental endocrine activity studies available for the butadiene styrene brominated copolymer although based on the large MW and structural groups, it is not expected to have endocrine activity due to its limited bioavailability and inability to be readily metabolized in the body.

Chemical Alternatives and the Toxic Substances Control Act

EPA's Design for the Environment (DfE) program is administered by the Office of Pollution Prevention and Toxics (OPPT), which is charged with the implementation of the Toxic Substances Control Act (TSCA) and the Pollution Prevention Act (PPA).

Central to the administration of TSCA is the management of the TSCA Inventory. Section 8 (b) of TSCA requires EPA to compile, keep current, and publish a list of each chemical substance that is manufactured or processed in the United States. Companies are required to verify the TSCA status of any substance they wish to manufacture or import for a TSCA-related purpose. For more information, please refer to the TSCA Chemical Substance Inventory website: http://www.epa.gov/opptintr/existingchemicals/pubs/tscainventory/basic.html

TSCA and DfE Alternatives Assessments

Substances selected for evaluation in a DfE Alternatives Assessment generally fall under the TSCA regulations and therefore must be listed on the TSCA inventory, or be exempt or excluded from reporting before being manufactured in or imported to, or otherwise introduced in commerce in, the United States. For more information see http://www.epa.gov/oppt/newchems/pubs/whofiles.htm.

To be as inclusive as possible, DfE Alternatives Assessments may consider substances that may not have been reviewed under TSCA and therefore may not be listed on the TSCA inventory. DfE has worked with stakeholders to identify and include chemicals that are of interest and likely to be functional alternatives, ***regardless of their TSCA status.*** Chemical identities are gathered from the scientific literature and from stakeholders and, for non-confidential substances, appropriate TSCA identities are provided.

Persons are advised that substances, including DfE identified functional alternatives, may not be introduced into US commerce unless they are in compliance with TSCA. Introducing such substances without adhering to the TSCA provisions may be a violation of applicable law. Those who are considering using a substance discussed in this report should check with the manufacturer or importer about the substance's TSCA status. If you have questions about reportability of substances under TSCA, please contact the Industrial Chemistry Branch at 202-564-8740.

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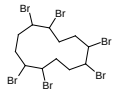
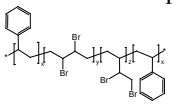
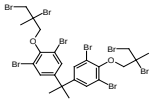
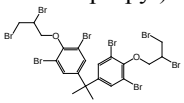
4.7 Hazard Summary Table

Table 4-4. Hazard Summary for HBCD and Alternatives

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

d This hazard designation would be assigned MODERATE for a potential for lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations.
§ Based on analogy to experimental data for a structurally similar compound.
¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical For full chemical name and relevant trade names see the hazard profiles in Section 4.8	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization[1]	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Hexabromocyclododecane (HBCD) 	25637-99-4; 3194-55-6	L	*M*	L	M	H	*M*	M	L		VL	VL	VH	VH	H	VH
Butadiene styrene brominated copolymer¥ 	1195978-93-8	L	*L*	L	L	L	*L*	L[d]	L		M	L	*L*	*L*	*VH*	*L*
TBBPA-bis brominated ether derivative¥ 	97416-84-7	*L*[§]	*M*[§]	*M*[§]	*M*[§]	*M*[§]	*L*	*M*[§]	*L*[§]		*L*	*L*	*L*	*L*	*H*	*H*
TBBPA bis(2,3-dibromopropyl) ether ¥ 	21850-44-2	L	*M*	M	*M*	*M*	*L*	*M*	L		L	L	L	*L*	VH	*H*

[1] At this time, there are no standard test methods for respiratory sensitization and no test data; as a result there was no designation for this endpoint.

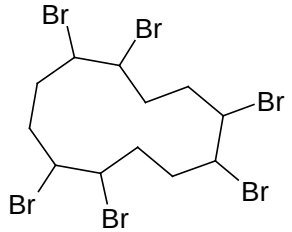
4.8 Hazard Profiles

Hexabromocyclododecane (HBCD)

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Hexabromocyclododecane (HBCD)	25637-99-4; 3194-55-6	L	*M*	L	M	H	*M*	M	L		VL	VL	VH	VH	H	VH

Hexabromocyclododecane (HBCD)



Representative structure; substitution and stereochemistry not specified

CASRN: 25637-99-4; 3194-55-6

MW: 641.70

MF: $C_{12}H_{18}Br_6$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: BrC1CC(CC(CC(CC(CC(C1)Br)Br)Br)Br)Br (for CASRN 25637-99-4); BrC(C(Br)CCC(Br)C(Br)CCC(Br)C(Br)C1)C1 (for CASRN 3194-55-6)

Synonyms: Cyclododecane, hexabromo- (CA Index Name for CASRN 25637-99-4); Cyclododecane, 1,2,5,6,9,10-hexabromo- (CA Index Name for CASRN 3194-55-6); HBCD; HBCDD

Trade Names: BRE 5300 Pyroguard F 800; Bromkal 73-6CD; Pyroguard SR 103; CD 75; Pyroguard SR 103A; CD 75P; Pyrovatex 3887; FR 1206; Safron 5261; FR 1206HT; Saytex HBCD; HBCD-LM; Saytex HBCD-LM; HBCD-LMS; Saytex HBCD-SF; Myflam 11645; Saytex HP 900; Nicca Fi-None CG 1; SR 103; Nicca Fi-None TS 1; SR 104; Nicca Fi-None TS 3; YM 88

Chemical Considerations: This is a discrete organic chemical with a MW <1,000. There are 16 possible hexabromocyclododecane (HBCD) isomers. CASRN 25637-99-4 is assigned to a non-specific mixture of all HBCD isomers and CASRN 3194-55-6 is assigned to the mixture of 1,2,5,6,9,10- HBCD isomers. There are differences in the fate, the behavior in the environment and the potential for toxic effects for individual HBCD isomers; therefore, studies identifying specific isomers are labeled in this assessment. Technical HBCD is predominantly comprised of three diastereomers (these are isomers that differ only in the three-dimensional orientations of the bromine substituents), known as α-, β- and γ- HBCD. Additionally, EPI v 4.1 was used to estimate physical/chemical and environmental fate values in the absence of experimental data. EPI-estimated values for HBCD are not isomer specific; the estimations were considered to be applicable to all isomers. Measured values from experimental studies were incorporated into the estimations. The overall hazard designations in this profile were determined using a conservative approach; each designation was based on the most hazardous material or value in the event that there were multiple adequate, high-quality measured values reported.

On August 18, 2010, EPA released an action plan on this brominated flame retardant category, hexabromocyclododecane, which outlined the Agency concerns for these chemicals and proposed risk management approaches to address those concerns, including a list of potential future regulatory actions (http://www.epa.gov/oppt/existingchemicals/pubs/actionplans/hbcd.html). One such regulatory action has already been initiated. In the spring of 2012, EPA proposed a Significant New Use Rule (SNUR) to enable EPA to review future use of HBCD in consumer textiles. If finalized, the rule will require that anyone intending to manufacture, import, or process HBCD for use in consumer textiles to notify EPA. The notification would provide EPA with an opportunity to evaluate the health and environmental effects of using HBCD in consumer textiles (www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2011-0489-0001). Other regulatory actions are being considered.

Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: Tetrabromocyclododecene, dibromocyclododecadiene and 1,5,9-cyclododecatriene by aerobic and anaerobic degradation (ECHA, 2008).	
Analog: No analogs **Endpoint(s) using analog values:** Not applicable	**Structure:** Not applicable
Structural Alerts: Cyclic halogenated hydrocarbons, neurotoxicity; halogenated aliphatic hydrocarbons, potential nephrotoxins (EPA, 2011)	
Risk Phrases: R63 - Possible risk of harm to the unborn child; R64 - May cause harm to breastfed babies (NICNAS, 2012)	
Hazard and Risk Assessments: A risk assessment was prepared for HBCD by the National Academy of Sciences National Research Council (NAS, 2000) and European Communities (EINECS, 2008; SCHER, 2008a; SCHER, 2008b). A Screening Assessment was prepared by Environment Canada/Health Canada (Environment Canada, 2011), the Australian National Industrial Chemicals Notification and Assessment Scheme (NICNAS, 2012) and an OECD Screening Information Dataset Initial Assessment Profile (SIAP) was completed in 2007 (OECD, 2007). HBCD was also part of the Initial Risk-Based Prioritization of High Production Volume Chemicals (HPV) (EPA, 2008).	

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	185-195 (Measured)	NAS, 2000	Similar values are consistently reported in secondary sources.
	172-184 to 201-205; 190 (average) (Measured)	EINECS, 2008	
	180-185 (Measured)	NICNAS, 2012	
	175-195 (Measured)	IUCLID, 2000	
Boiling Point (°C)	>190 (decomposes) (Measured)	EINECS, 2008; NICNAS, 2012	Value reported in a secondary source.
Vapor Pressure (mm Hg)	$4.7x10^{-7}$ at 21ºC (Measured) GLP Spinning Rotor Method/OECD TG 104 and EPA OPPTS 830.7952; reported as $6.3x10^{-5}$ Pa HBCD sample consisted of 8.5%, 6.0% and 79.1% α-, β- and γ-HBCD respectively.	EINECS, 2008; NICNAS, 2012	The method used is not recommended for substances with vapor pressures $<10^{-4}$ Pa (or 0.0008 mm Hg). However, this value indicates a low vapor pressure.
	α-HBCD 7.9×10^{-11} β-HBCD 4.4×10^{-11} γ-HBCD 6.3×10^{-13} at 25 ºC Gas saturation method (Measured)	Kuramochi et al., 2010	The method used is not recommended for substances with vapor pressures outside of 7.5×10^{-10} to 0.008 mm Hg. This value indicates a low vapor pressure.
Water Solubility (mg/L)	$6.6x10^{-2}$ at 20ºC (Measured) GLP Column Elution Method α-HBCD: $4.8x10^{-2}$ β-HBCD: $1.5x10^{-2}$ γ-HBCD: $2.1x10^{-3}$	EINECS, 2008; NICNAS, 2012	Value reported in a secondary source. The value reported is the sum of the water solubility values for individual diastereomers found in the technical mixture.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	0.12 (Measured) Solubility value of total HBCD One isomer: α-HBCD: 1.4×10^{-2} β-HBCD: 2.8×10^{-3} γ-HBCD: 1.5×10^{-3} Mixture of isomers (technical product): α-HBCD: 8.1×10^{-2} β-HBCD: 3.3×10^{-2} γ-HBCD: 1.6×10^{-3} Direct Coupled Column Linked Chromatographic Technique	Kuramochi et al., 2007	The value reported is the sum of the water solubility values for individual diastereomers found in the technical mixture.
	0.008 (Measured)	IUCLID, 2000	Value reported in a secondary source.
	3.4×10^{-3} at 25ºC (Measured) GLP Column Elution Method	EINECS, 2008; NAS, 2000; NICNAS, 2012	The measurement was performed on the technical product, which was not 100% pure. The value reported was for a single diastereomer (γ-HBCD) in the mixture.
	8.6×10^{-3} at 25ºC (Measured; CASRN 3194-55-6)	HSDB, 2011a	Value reported in a secondary source; sufficient details were not available to assess the quality of this study.
Log K_{ow}	5.62 (Measured) GLP Generator Column Method	EINECS, 2008; NICNAS, 2012	The measurement was performed on the technical product, which was not 100% pure.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	One isomer: α-HBCD: 5.8 β-HBCD: 5.8 γ-HBCD: 6.3 Mixture of isomers (technical product): α-HBCD: 5.7 β-HBCD: 6.1 γ-HBCD: 6.3 Slow-stirrer method (Measured)	Kuramochi et al., 2007	Adequate non-guideline study.
	5.81 (Measured)	IUCLID, 2000	Value reported in a secondary source.
Flammability (Flash Point)	Not flammable (Estimated)	EINECS, 2008	Value reported in a secondary source.
Explosivity	Not explosive (Estimated)	EINECS, 2008	Value reported in a secondary source.
Pyrolysis	Decomposition occurs between 240 and 270°C; study performed in a batch reactor with inert and oxidizing atmospheres Numerous products were identified by gas chromatography/mass spectrometry (GC/MS), proposed pyrolysis degradation products were non-brominated structures and brominated structures	Barontini et al., 2001; NICNAS, 2012	Adequate non-guideline study. Potential mechanisms for thermal decomposition proposed.
pH	Not applicable	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable	Professional judgment	Dissociation is not expected; the chemical does not contain ionizable functional groups.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**HBCD is readily absorbed following oral administration in rodent studies and is distributed primarily to lipid-rich tissues. Smaller amounts of HBCD have been detected in the lungs, kidneys, blood, and brain. HBCD and its metabolites are eliminated from the body mainly in the feces (~30 -70%) and in urine (~16%). Dermal absorption is estimated to be 4% for fine particles and 2% for granular particles. The overall extent of metabolism of technical-grade HBCD is unknown. Three polar metabolites have been detected following exposure to γ-HBCD. It has been demonstrated in monitoring studies with volunteers that HBCD may be transferred across the placenta to the developing fetus and secreted in breast milk during lactation.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Rats (2 males, 8 females) administered a single oral dose of 1.93 mg radiolabeled HBCD eliminated 86% of the dose within 72 hours (70% in feces and 16% in urine) Absorption is quick from the gastrointestinal tract with a half-life of 2 hours (absorbed fraction not reported); elimination is slower in adipose tissue as opposed to non-adipose tissue	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Authors state that caution is urged in interpreting the data due to the small sample size and the brief nature of the final report.
		Four male Wistar rats orally administered 500 mg/kg-day HBCD in olive oil for 5 days Average daily rate of excretion in the feces was 29-37% of the dose; the cumulative excretion was constant at 32-35%; urinary excretion was not observed; metabolites were not detected in the urine or feces; HBCD was detected only in adipose tissue (0.3-0.7 mg/g fat)	EPA, 2005; NICNAS, 2012	Reported in a secondary source.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		In rodents, HBCD is readily absorbed through the gastrointestinal tract with highest concentrations in adipose tissue and muscle, followed by the liver; it has been found in much lower concentrations in the lungs, kidneys, blood and brain Oral absorption estimated to be 50-100%; accumulation of α-diastereomer is much higher than other diastereomers Overall extent of metabolism of technical-grade HBCD is unknown; γ-HBCD is metabolized to form three polar metabolites EU risk assessment concluded 4% dermal absorption for fine particles and 2% for granular particles	ECHA, 2008	Reported in a secondary source with limited study details.
		Following continuous exposure (via homes, offices and cars), HBCD was detected in human adipose tissue and blood HBCD may be transferred across the placenta and via breast milk; estimates of uptake via breast milk range from 50 to 100%; intake of HBCD via breast milk is 1.5 ng/kg body weight/day for 0-3-month-old babies and 5.6 ng body weight/day for 3-12-month-old babies	Marvin et al., 2011	Reported in a secondary source with limited study details.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Acute Mammalian Toxicity		**LOW: Based on acute oral and dermal LD_{50} values >2,000 mg/kg in rats and rabbits and an acute inhalation LC_{50} >200 mg/L in rats.**		
Acute Lethality	**Oral**	Rat LD_{50} >10,000 mg/kg	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details.
		Rat LD_{50} >6,400 mg/kg	EINECS, 2008	Reported in a secondary source. Non-guideline study. Dose and particle size not reported; 7-day observation period.
	Dermal	Rabbit LD_{50} >8,000 mg/kg	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details.
		Rabbit LD_{50} >20,000 mg/kg	EINECS, 2008; NICNAS, 2012	Non-guideline study. Too few animals were used; clinical signs not reported.
	Inhalation	Rat LC_{50} >200 mg/L	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details.
		Acute respiratory irritation test in Charles River CD rats (5/sex) exposed (whole-body) to 202 mg/L HBCD dust for 4 hours Slight dyspnea, which did not persist into the 14-day observation period; no deaths occurred and there were no signs of respiratory tract irritation	EINECS, 2008; NICNAS, 2012	Reported in a secondary source. Non-guideline study. No autopsy was performed. According to OECD guidelines (436), starting concentrations for dust should be 0.05–5 mg/L.
Carcinogenicity		**MODERATE: Only one carcinogenicity study was located. In this mouse dietary study, there were increases in tumor incidence compared to controls. This study is not adequate to determine a hazard designation for the carcinogenicity endpoint due to high tumor incidence in control males. Carcinogenic potential cannot be ruled out therefore an estimated Moderate hazard is designated.**		
	OncoLogic Results			This compound is not amenable to available estimation methods.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Carcinogenicity (Rat and Mouse)	Lifetime (18-month) dietary bioassay in B6C3F1 mice (50/sex/dose) Doses: 0, 100, 1,000 or 10,000 ppm for 18 months No adverse effect on mortality, clinical signs, body weight or food consumption Gross lesions/nodules detected at necropsy (hepatocyte swelling, degeneration, necrosis, vacuole formation and fatty infiltration) were not considered dose-related; Incidence of hepatocellular tumors were reported in males: 14/50, 19/50, 27/50, 15/50 in the 0, 100, 1,000, and 10,000 ppm groups, respectively and in females: 0/50, 1/50, 1/50, 5/50 in the 0, 100, 1,000, and 10,000 ppm groups, respectively. The study author stated that there was no correlation between dose and incidence of hepatic tumors for both male and female mice; the number of tumors in this study were within the historical rates of spontaneously induced tumors in control animals in this strain of mice	Kurokawa et al., 1984; EINECS, 2008; EPA, 2005; NICNAS, 2012	Study not conducted according to OECD guidelines; this study is not adequate to determine a hazard designation for the carcinogenicity endpoint.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		HBCD does not meet criteria (NOHSC, 2004) for classification as a carcinogen (R45, R49, R40)	NICNAS, 2012	Reported in a secondary source.
	Combined Chronic Toxicity/ Carcinogenicity			No data located.
Genotoxicity		**LOW: Based on negative results for gene mutations in bacterial cells, a lack of chromosomal aberrations in human peripheral blood lymphocyte cells *in vitro,* and negative results in recombination and mouse micronucleus tests.**		
	Gene Mutation *in vitro*	Negative in *Salmonella typhimurium* (strains not specified) in the presence and absence of metabolic activation	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative, mammalian chromosomal aberration test with human peripheral blood lymphocytes in the presence and absence of metabolic activation Doses: 10, 19, 38, 75, 150, 300 and 600 µg/mL	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines, and GLP.
	DNA Damage and Repair			No data located.
	Other *in vitro*	Positive, intragenic recombination test in Sp5/V79 and SPD8 hamster cells; cell lines developed by study authors Doses: 2-20 µg/mL	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Non-guideline study. Not a standard test used by regulatory agencies to assess genotoxicity. Reliability and predictive ability is unknown.
		Negative, mouse micronucleus test Doses: 0, 500, 1,000 or 2,000 mg/kg in dimethyl sulfoxide (DMSO)	EPA, 2005	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects	**MODERATE: Based on a LOAEL of 138 mg/kg-day for reduced number of primordial follicles in F_1 females in a two-generation dietary study in rats. There is uncertainty in that reproductive effects may occur at doses between the identified NOAEL (14.3 mg/kg-day) and the LOAEL (138 mg/kg-day).Using a conservative approach, a MODERATE hazard is designated. There were no treatment-related effects on the fertility index, sperm parameters, estrous cyclicity, reproductive organ weights or histopathology in F_0 or F_1 adults.**		

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Reproduction/ Developmental Toxicity Screen	Two-generation dietary (HBCD particles in ground food) study in Crl:CD (SD) rats (24/sex/group) Doses: 0, 150, 1,500 or 15,000 ppm Mean daily intake during entire administration: 10.2, 101 and 1,008 mg/kg-day (F_0 males); 14, 141 and 1,363 mg/kg-day (F_0 females); 11.4, 115 and 1,142 mg/kg-day (F_1 males); and 14.3, 138 and 1,363 mg/kg-day (F_1 females) Delayed eye opening and surface righting reflex response (F_1 and F_2 pups) that were not consistent over generations or sexes (not considered dose-related) Decreased number of primordial ovarian follicles (30% at 1,500 and 15,000 ppm) in F_1 generation (control: 316.3 ± 119.5; 14.3 mg/kg-day: 294.2 ± 66.3; 138 mg/kg-day: 197.9 ± 76.9). No significant effects in copulation index, gestation index, pre-coital interval, number of implantations, delivery index or number of pups delivered in either F_0 or F_1 animals NOAEL = 14.3 mg/kg-day LOAEL = 138 mg/kg-day (based on reduced number of primordial ovarian follicles in F_1 females)	Ema et al., 2008 (as cited in EINECS, 2008; NICNAS, 2012)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD 416 guidelines and GLP. HBCD particles were mixed with ground dry feed at the reported concentrations; bioavailability may be dependent on particle size and dose. Study does not consider litter effects; It is noted that the number of primordial cells in background control data was 189.5 – 353.4 (mean = 295.6) in 4 studies (10 females/study) in studies conducted in 2005-2006. While the number of primordial cells was variable within these studies, the 30% treatment-related decrease at the 138 mg/kg-day dose level compared to controls in this study, is a significant decrease; in addition, the decrease at 198 mg/kg dose suggests a dose-response.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects	28-Day gavage study in Sprague-Dawley rats (10/sex/group) Doses: 0, 1, 2.5 and 5% (0, 940, 2,410 and 4,820 mg/kg-day) Very slight change of numerical development of the follicles and ripening follicles in the ovaries (4,820 mg/kg); normal differentiation in the testes and epididymides with undisturbed spermiohistogenesis (high-dose males) No NOAEL/LOAEL reported	Zeller and Kirsch, 1969 (as cited in EINECS, 2008; EPA, 2005; NICNAS, 2012)	Unpublished laboratory report, described in a secondary source. Non-guideline study; EINECS (2008) states that this study was not carried out in accordance with present standards.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		90-Day gavage study in Crl:CD(SD) IGS rats (15/sex/group) Doses: 0, 100, 300 and 1,000 mg/kg-day No changes to the estrus cycle or to sperm motility/viability, morphology or number No treatment-related changes in weight or microscopic effects in the reproductive organs with the exception of an increase in mean prostate weight (1,000 mg/kg-day) on day 90; relative prostate weight was also increased on day 90 compared with controls; there were no statistically significant differences in prostate weights between the control and treated groups following the recovery period (28 days post exposure) NOAEL = 1,000 mg/kg-day (highest dose tested LOAEL = Not established	Chengelis, 2001 (as cited in EPA, 2005; NICNAS, 2012)	Unpublished laboratory report, described in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**HIGH: Based on a LOAEL of 13.5 mg/kg-day (NOAEL = 0.9 mg/kg) in mice for reduced habituation, decreased locomotion, and decreased rearing in neonatal male mice exposed to HBCD on postnatal day (PND) 10. In addition, hearing appeared to be impaired at low frequency ranges following exposure to HBCD at doses estimated to be as low as 0.2 mg/kg-day (BMD_{05} = 1.0 mg/kg-day) in adult rats exposed via diet from pre-mating to after weaning. Other neurodevelopmental effects occurred at higher doses. Reduced density of brain CNPase-positive oligodendrocytes was observed in a dietary study in rats exposed to HBCD from gestation day (GD) 10 until postnatal day (PND) 20 at a dose >1,000 mg/kg-day. A LOAEL of 1504.8 mg/kg-day (time weighted average) was identified in this study for thyroid effects (increased thyroid weight and decreased serum triiodothyronine [T3] concentrations).There is uncertainty in that these thyroid effects may occur at doses between the identified NOAEL (146.3 mg/kg-day) and the identified LOAEL (1504.8 mg/kg-day). Benchmark dose (BMD) modeling was conducted to predict at which dose these effects could occur. A $BMDL_{SD1}$ of 73 mg/kg-day for decreased serum T3 levels was predicted, which falls within the criteria for a Moderate hazard designation. A dose-dependent increase in F_2 pup mortality was also observed at 15,000 ppm (1,363 mg/kg-day). Also, in a two-generation dietary study in rats, delayed eye opening was observed in F_1 and F_2 pups; however, this effect was not consistent over generations or sexes and was not considered to be dose-related. No developmental effects were observed in two other prenatal exposure studies at oral doses ≥ 500 mg/kg-day.**		
	Reproduction/ Developmental Toxicity Screen	Dietary study in pregnant Crj:CD rats; Doses: 0, 100, 1,000 or 10,000 ppm (0, 8.1-21.3, 80.7-212.9 or 803.2-2,231.3 mg/kg-day) from gestation day (GD) 10 until postnatal day (PND) 20 Time-weighted average (TWA) doses: 0, 14.8, 146.3 and 1,504.8 mg/kg-day Maternal toxicity: increased relative thyroid weights Trend for an increase in the incidence of thyroid follicular cell hypertrophy at 100 and 1,000 ppm (TWA dose 14.8 and 146 mg/kg-day, respectively) in dams; statistically significant at 10,000 ppm	Saegusa et al., 2009	Lowest end of maternal exposure range used to determine LOAEL and NOAEL values for maternal and developmental toxicity and thus, hazard. TWA doses were calculated by multiplying the HBCD intake (mg/kg-day) by the number of inclusive days of exposure for each time point. The sum of each time point for an individual dietary concentration (100, 1,000 and 12,000 ppm) was divided by the total number of inclusive days (33 days) of exposure.

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PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		(TWA dose 1,504.8 mg/kg-day) Developmental toxicity: No abnormalities in clinical observation in offspring; increased relative liver weight; weak hypothyroidism with increased thyroid weight, increased incidence of thyroid follicular cell hypertrophy, increased thyroid stimulating hormone [TSH] concentrations and decreased T3 concentrations at 10,000 ppm (TWA dose 1,504.8 mg/kg-day); reduced density of CNPase-positive oligodendrocytes at 10,000 ppm (TWA dose 1,504.8 mg/kg-day) Increased thyroid weight and decreased serum T3 concentrations when male offspring reached adult stage at 1,000 ppm (TWA dose 146.3 mg/kg-day) Maternal: NOAEL = 1,000 ppm (146.3 mg/kg-day LOAEL = 10,000 ppm (1504.8 mg/kg-day, (based on increased incidence of thyroid follicular cell hypertrophy) Developmental: NOAEL = 100 ppm (14.8 mg/kg-day) LOAEL = 1,000 ppm (146.3 mg/kg-day, based on thyroid effects) BMD_{SD1} = 119.68 mg/kg-day (based on decreased serum T3 levels) $BMDL_{SD1}$ = 73.53 mg/kg-day	Saegusa et al., 2009 (continued)	Dosing administered from gestation day (GD) 10 to postnatal day (PND) 20 = GDs 10-20: 0, 8.1, 80.7 and 803.2 mg/kg-day; PNDs 1-9: 0, 14.3, 138.7 and 1,404.8 mg/kg-day; PNDs 9-20: 0, 21.3, 212.9 and 2,231.3 mg/kg-day (described in study report). In an effort to predict at what dose effects would occur, BMD modeling was conducted on the datasets for changes in serum T3 levels and for changes in thyroid weight. The BMD and BMDL for a change of 1 standard deviation from the control for decreased serum T3 levels were predicted to be 119.68 and 73.53 mg/kg-day, respectively (see Table 1 at end of profile). The data for changes in thyroid weight were determined not to be suitable for BMD modeling (Table 2). It is not clear if effects on brain CNPase-positive oligodendrocytes are predictive for functional effects. Thyroid weights were not recorded on PND 20. There is generally a typically high variance in TSH levels; changes in point measurements of

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
			Saegusa et al., 2009 (continued)	thyroid hormone are more indicative of altered thyroid function when observed with changes in thyroid weight and histopathology.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Two-generation dietary study in Crl:CD(SD) rats (24/sex/group) Doses: 0, 150, 1,500 or 15,000 ppm (10-14, 101-141 or 1,008-1,363 mg/kg-day) Mean daily intake during entire administration: 10.2, 101 and 1,008 mg/kg-day (F_0 males); 14, 141 and 1,363 mg/kg-day (F_0 females); 11.4, 115 and 1,142 mg/kg-day (F_1 males); and 14.3, 138 and 1,363 mg/kg-day (F_1 females) No effect on spontaneous locomotor activity (10 min intervals for a total of 60 min; F_1 pups). No difference between controls and treated F_1 rats on day 1 of the T-maze test. On day 3 of T-maze, males performed better than controls (shorter elapsed time at 1,500 and 15,000 ppm with fewer errors at 15,000 ppm), but no difference between controls and females. Delayed eye opening and surface righting reflex response (F_1 and F_2 pups) that was not consistent over generations or sexes (not considered dose-related); dose-dependent pup mortality during lactation (F_2, 35% at 15,000 ppm) NOAEL = 138 mg/kg-day LOAEL = 1,363 mg/kg-day (based on increased pup mortality during lactation in offspring from F_1 dams)	Ema et al., 2008 (as cited in EINECS, 2008; NICNAS, 2012)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP. HBCD particles were mixed with ground dry feed at the reported concentrations. Bioavailability may be dependent on particle size and dose. Study does not consider litter effects.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Wistar rats were exposed via the diet before conception, through mating, gestation, lactation and after weaning Doses: 0, 0.1, 0.3, 1, 3, 10, 30 and 100 mg/kg-day There were no treatment-related changes in number of implantations, litter size, and sex ratio compared to controls Effects on lower frequency range in 140-day old male offspring; no progressive delays in peak latencies were detected in later waves of the brainstem auditory evoked potentials (BAEP), suggesting a cochlear origin of hearing impairment. Decreased latencies to movement onset were reported in all three situations (bar, grid, box) used to measure haloperidol-induced cataleptic behavior in 110-day old female rats in the 30 and 100 mg/kg-day dose groups at testing times 30 and 60 minutes. The BMD and BMDL for the sum of latencies in female rats were 15.6 and 3.7 mg/kg-day, respectively. Male rats exhibited a significant latency only for foreleg retraction on the box at the 60 minute test time (BMD and BMDL = 10.8 and 3.0 mg/kg-day, respectively) BMD_{05} = 1.0 $BMDL_{05}$ = 0.2 mg/kg-day (based on hearing impairment)	Lilienthal et al., 2006, 2009 (as cited in EINECS, 2008; NICNAS, 2012)	Guideline study. Conducted according to current EPA, OECD Guideline 415. BMD doses were calculated by the authors using a biologically relevant benchmark response of 5% deviation change from control; Rats were tested at 110 and 140 days old for the cataleptic and hearing impairment tests, respectively. It is difficult to determine, however, if the effect is due to developmental exposure to HBCD, a result of repeated-dose exposure, or a combination of the two. Due to this uncertainty, this study was not used to determine the hazard designation; however, the results of this study suggest that there is potential concern for neurotoxic effects.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development	Gavage study in pregnant Crl:CD(SD)IGS Br rats (25/group) Dose: 0, 250, 500 or 1,000 mg/kg-day from gestation days (GDs) 6 to 19 No maternal mortality or treatment-related effects on clinical signs, body weight gain or food consumption No effects on intrauterine growth/ survival; no treatment-related fetal malformations or developmental variations. NOAEL (maternal/developmental): 1,000 mg/kg-day (highest dose tested) LOAEL = Not established	Stump, 1999 (as cited in EINECS, 2008; EPA, 2005; NICNAS, 2012)	Unpublished laboratory report, described in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP. There were no effects at the highest dose tested; a LOAEL was not identified.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Dietary study in pregnant rats Doses: 0, 0.01, 0.1 or 1% HBCD on gestation days (GDs) 0-20; authors estimate doses in the feed were equivalent to 0, 5, 50 or 500 mg HBCD/kg body weight-day No effects on maternal weight gain or food consumption and no gross appearance of internal organs No adverse effects on corpora lutea, implants, resorptions, live fetuses, sex ratio or body or placental weight and no fetal deaths; no external, skeletal or visceral malformations were detected; a few skeletal variations were present, but were of similar type noted in controls and not considered statistically significant Normal development in neonates carried through to 6 weeks of age NOAEL = 1% (500 mg/kg-day, highest dose tested) LOAEL = Not established	Murai et al., 1985 (as cited in EPA, 2005; NICNAS, 2012)	Reported in secondary sources. EPA (2005) refers to KEMI, who deemed this study to be insufficient. There were no effects at the highest dose tested; a LOAEL was not identified. Same study described in EINECS (2008) with variations on calculated doses: Doses equivalent to: 0, 7.5, 75 and 750 mg/kg-day (based on assumption that animals mean weight is 200 g and food consumption is 15 g/day) NOAEL (fetal) = 750 mg/kg-day NOAEL (maternal) = 75 mg/kg-day based on 13% liver weight increase at the high dose.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Postnatal Development	Gavage study in neonatal male NMRI mice (8-10/group) Doses: 0.9 or 13.5 mg/kg dissolved in a mixture of egg lecithin and peanut oil on PND 10 Reduced habituation with initial hypoactivity followed by hyperactivity in a novel environment; decreased locomotion and rearing during first 20 minutes with no effects in later measurements NOAEL = 0.9 mg/kg LOAEL = 13.5 mg/kg (based on reduced habituation, decreased locomotion, and rearing)	Eriksson et al., 2006 (as cited in EINECS, 2008; NICNAS, 2012)	Reported in a secondary source. Non-guideline study. Study used too few dose groups and the behavioral alterations were induced at doses that did not produce clinical signs or affect weight gain. Though the Eriksson et al., 2006 study was a non-guideline study, it was adequate to use for assessing neurodevelopmental effects; exposure occurred during the peak period of rapid brain growth and the methodology was validated with known neurotoxic agents in previous studies. Effects due to litter size were not taken into consideration.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**MODERATE: Estimated to have potential for neurotoxicity based on structural alert for cyclic halogenated aliphatic hydrocarbons and professional judgment. No adverse effects were noted in functional observation battery (FOB) and motor activity tests at doses ≤1,000 mg/kg-day (highest dose tested) in adult animals. In another study, hearing appeared to be impaired at low frequency ranges following exposure to HBCD at doses estimated to be as low as 0.2 mg/kg-day in adult rats exposed from pre-mating to after weaning; uncertainty exists as to whether the effects were a result of gestational/developmental exposure or repeated dose exposure to HBCD therefore it does not influence the adult neurotoxicity hazard designation.**		
	Neurotoxicity Screening Battery	Potential for producing neurotoxicity (Estimated)	EPA, 2011	Estimated based on structural alert for cyclic halogenated aliphatic hydrocarbons.
		90-Day gavage study in Crl:CDC(SD)IGS rats (15/sex/group) Doses: 0, 100, 300 and 1,000 mg/kg-day at a dosage volume of 5 mL/kg in corn oil; test article was a composite of three lots of commercial HBCD No adverse results in functional observation battery and motor activity tests NOAEL = 1,000 mg/kg-day (highest dose tested) LOAEL = Not established	Chengelis, 2001 (as cited in EPA, 2005; NICNAS, 2012)	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP.
		In vitro plasma membrane uptake study in removed brains of male Wister rats Doses: 2-20 µM Inhibition of neurotransmitter uptake into synaptosomes, dopamine uptake into synaptic vesicles and glutamate uptake at low concentrations	Mariussen and Fonnum, 2003 (as cited in EINECS, 2008; NICNAS, 2012)	Study reported in a secondary source.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Neurodevelopmental	Wistar rats were exposed via the diet before conception, through mating, gestation, lactation and after weaning Doses: 0, 0.1, 0.3, 1, 3, 10, 30 and 100 mg/kg-day There were no treatment-related changes in number of implantations, litter size, and sex ratio compared to controls Effects on lower frequency range in 140-day old male offspring; no progressive delays in peak latencies were detected in later waves of the brainstem auditory evoked potentials (BAEP), indicating a cochlear origin of hearing impairment. Decreased latencies to movement onset was reported in all three situations (bar, grid, box) used to measure haloperidol-induced cataleptic behavior in 110-day old female rats in the 30 and 100 mg/kg-day dose groups at testing times 30 and 60 minutes. The BMD and BMDL for the sum of latencies in female rats were 15.6 and 3.7 mg/kg-day, respectively. Male rats exhibited a significant latency only for foreleg retraction on the box at the 60 minute test time (BMD and BMDL = 10.8 and 3.0 mg/kg-day, respectively) BMD_{05} = 1.0 $BMDL_{05}$ = 0.2 mg/kg-day (based on hearing impairment)	Lilienthal et al., 2006, 2009 (as cited in EINECS, 2008; NICNAS, 2012)	Guideline study. Conducted according to current EPA, OECD Guideline 415. BMD doses were calculated by the authors using a biologically relevant benchmark response of 5% deviation change from control. Rats were tested at 110 and 140 days old for the cataleptic and hearing impairment tests, respectively. It is difficult to determine, however, if the effect is due to developmental exposure to HBCD, a result of repeated-dose exposure, or a combination of the two. Due to this uncertainty, this study was not used to determine the hazard designation; however, the results of this study suggest that there is potential for neurotoxic effects.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Repeated Dose Effects	**MODERATE: Based on increased TSH levels in F_0 female rats at an oral dose of 14 mg/kg-day (lowest dose tested) in a two-generation dietary study. In a developmental study in rat dams exposed from gestation day (GD) 10 until postnatal day (PND) 20, increased thyroid weights and increased incidence of thyroid follicular cell hypertrophy were observed at 146.3 mg/kg-day (NOAEL= 14.8 mg/kg-day). Repeat dose studies reported liver effects including increased liver weights in conjunction with histopathological findings in a 90-day gavage study in rats administered 100 mg/kg-day (lowest dose tested) and increased liver weights in a 28-day gavage study in rats at a dose of 940 mg/kg-day (lowest dose tested). In the 28-day study, effects on the thyroid (microfollicular hyperplasia and increased activity of the thyroid epithelium) also occurred at 940 mg/kg-day and were attributed to hypermetabolism as a result of increased thyroid activity. No significant adverse effects were noted in a 28-day gavage study in rats at doses up to 1,000 mg/kg-day; treatment-related liver effects noted in this study were mild, reversible and without effect on the clinical condition of the animals or associated with organ damage or diminished function. There is potential for nephrotoxicity based on a structural alert for halogenated aliphatic hydrocarbons.**		
	Potential for producing nephrotoxicity (Estimated)	EPA, 2011	Estimated based on a structural alert for halogenated aliphatic hydrocarbons.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Two-generation dietary study in Crl:CD(SD) rats (24/sex/group) Doses: 0, 150, 1,500 or 15,000 ppm (0, 10-14, 101-141 or 1,008-1,363 mg/kg-day) Mean daily intake during entire administration: 10.2, 101 and 1,008 mg/kg-day (F_0 males); 14, 141 and 1,363 mg/kg-day (F_0 females); 11.4, 115 and 1,142 mg/kg-day (F_1 males); and 14.3, 138 and 1,363 mg/kg-day (F_1 females) Increased serum TSH (F_0 females at 150 ppm and F_1 females at 15,000 ppm); decreased serum follicle stimulating hormone (FSH) levels in F_0 males and increased in F_0 females at 15,000 ppm; increased dihydrotestosterone (DHT) in F_1 males (15,000 ppm); increased incidence of decreased size of thyroid follicular cells in F_0 females (1,500 ppm) No significant differences in serum testosterone, estradiol, progesterone or luteinizing hormone (LH) levels Authors concluded that the effect on TSH levels is consistent through dose groups and generations, and is considered an effect of HBCD-exposure NOAEL = Not established LOAEL = 150 ppm (14 mg/kg-day, based on increased TSH levels in F_0 females; lowest dose tested)	Ema et al., 2008 (as cited in EINECS, 2008; NICNAS, 2012)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP. HBCD particles were mixed with ground dry feed at the reported concentrations; bioavailability may be dependent on particle size and dose. Study does not consider litter effects. Uncertainty exists concerning the extrapolation of the biological significance of thyroid effects between rodents and humans. There is uncertainty as to where effects may occur as this effect occurred at the lowest dose tested. It is possible that this effect could occur at a dose <10 mg/kg-day.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Dietary study in pregnant Crj:CD rats; Doses: 0, 100, 1,000 or 10,000 ppm (0, 8.1-21.3, 80.7-212.9 or 803.2-2,231.3 mg/kg-day) from gestation day (GD) 10 until postnatal day (PND) 20. Time weighted average (TWA) doses: 0, 14.8, 146.3 or 1,504.8 mg/kg-day Dams: increased relative thyroid weights; trend for an increase in the incidence of thyroid follicular cell hypertrophy at 100 and 1,000 ppm (TWA dose 14.8 and 146 mg/kg-day, respectively); statistically significant at 10,000 ppm (TWA dose 1,504.8 mg/kg-day) NOAEL = 100 ppm (14.8 mg/kg-day) LOAEL = 1,000 ppm (146.3 mg/kg-day, based on increased incidence of thyroid follicular cell hypertrophy)	Saegusa et al., 2009	Lowest end of maternal exposure range used to determine LOAEL and NOAEL values for repeated-dose toxicity and thus, hazard. Time weighted average (TWA) doses were calculated by multiplying the HBCD intake (mg/kg-day) by the number of inclusive days of exposure for each time point. The sum of each time point for an individual dietary concentration (100, 1,000 and 12,000 ppm) was divided by the total number of inclusive days (33 days) of exposure. Dosing administered from gestation day (GD) 10 to postnatal day (PND) 20 = GDs 10-20: 0, 8.1, 80.7 and 803.2 mg/kg-day; PNDs 1-9: 0, 14.3, 138.7 and 1,404.8 mg/kg-day; PNDs 9-20: 0, 21.3, 212.9 and 2,231.3 mg/kg-day (described in study report).

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	90-Day gavage study in Crl:CD (SD)IGS rats (15/sex/group) Doses: 0, 100, 300 and 1,000 mg/kg-day at a dosage volume of 5 mL/kg in corn oil; test article was a composite of three lots of commercial HBCD Increase in liver weight (100 mg/kg-day) with mild histopathological findings (minimal hepatocellular vacuolation, minimal to mild hepatocellular hypertrophy). Minimal thyroid follicular cell hypertrophy (1,000 mg/kg-day); it is not apparent if these changes were related to treatment (authors state that changes may have been a related to reduced serum thyroxine [T4] levels, which is a normal physiological response of healthy organisms acting to maintain serum T4 levels in the normal range) No clinical signs of toxicity and no adverse effects on survival, food consumption, body weight or hematological parameters; no article-related ocular lesions; no adverse results in functional observation battery and motor activity tests; no changes to the estrus cycle or to sperm motility/viability, morphology or number; no gross lesions NOAEL = Not established LOAEL = 100 mg/kg-day (based on increased liver weight in conjunction with histopathological findings; lowest dose tested)	Chengelis, 2001 (as cited in EPA, 2005; NICNAS, 2012)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP. Commercial mixture composed of α isomer (6.3%), β isomer (9.1%) and γ isomer (76.9%). Study authors state that all test article-related changes were mild, reversible and generally secondary to hepatic enzyme induction (which is an adaptive not a toxic change) and without effect on the clinical condition of the animals or associated with specific target organ damage or diminished function; however, changes in liver weight in conjunction with histopathological can be considered an adverse effect.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	28-Day gavage study in Sprague-Dawley rats (10/sex/group) Doses: 0, 1, 2.5 and 5% (0, 940, 2,410 and 4,820 mg/kg-day) Increased absolute and relative liver weights at all dose levels when compared to the control, but no microscopic pathology detected. Thyroid microfollicular hyperplasia and increased activity of the thyroid epithelium were reported at 1% (940 mg/kg-day); these effects were more marked at 2.5% (2,410 mg/kg-day) and very marked hyperplastic thyroid tissue with adenomatous proliferation and thyroid epithelial hyperactivity was reported at 5% (4,820 mg/kg-day); not specified if these effects occurred in the control group; very slight numerical development of the follicles and ripening follicles in the ovaries (4,820 mg/kg-day) Effects on the thyroid were attributed to hypermetabolism as a result of increased thyroid activity, and effects were not pathologic according to the study authors No clinical signs related to treatment or changes in any other organ; no change in clinical chemistry parameters Effects on the liver and thyroid were	Zeller and Kirsch, 1969 (as cited in EPA, 2005; NICNAS, 2012)	Non-guideline study; limited study details reported in a secondary source. The author's determination of the thyroid effects being non-pathologic in nature is based on the study author's judgment.

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PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	attributed to hyperactivity and hypermetabolism, respectively, and were not pathologic according to the study authors NOAEL = Not established LOAEL = 1% (940 mg/kg-day, based on increased liver weights; lowest dose tested)	Zeller and Kirsch, 1969 (as cited in EPA, 2005; NICNAS, 2012) (continued)	
	90-Day dietary study in Sprague-Dawley rats (20/sex/group) Doses: 0, 0.16, 0.32, 0.64 and 1.28% (0, 120, 240, 470 and 950 mg/-day) Increased incidence of hepatic lipoid phanerosis (fatty accumulation) in the liver was observed at all doses in a dose-dependent manner; however, there were no changes in liver clinical chemistry and no detectable histological changes; study authors noted that these effects were transient effects and attributed to increased activity in the liver No adverse clinical signs, changes in body weight or clinical chemistry parameters; no histological changes in any organ (other than the liver) NOAEL = 950 mg/kg-day (highest dose tested) LOAEL = Not established	Zeller and Kirsch, 1970 (as cited in EPA, 2005; NICNAS, 2012)	Unpublished laboratory report described in secondary sources. Guideline study. Was not conducted according to OECD guidelines. It is not specified where statistical significance for the increased incidence of liver effects occurs. Based on the limited observations reported, the NOAEL is determined (with low confidence) to be the highest dose tested (950 mg/kg-day).

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	28-Day gavage study in Sprague-Dawley rats (12 rats [6 of each sex] in the 125 and 350 mg/kg-day dose groups; 24 rats [12 of each sex] in the 1,000 mg/kg-day dose group) Doses: 0, 125, 350 or 1,000 mg/kg-day; at conclusion of the study 6 rats/sex in control and 1,000 mg/kg-day groups were sacrificed and necropsied while the remaining animals had a 14 day recovery period. Increased absolute liver weight (1,000 mg/kg-day in males, 350 and 1,000 mg/kg-day in females); increased relative liver weight at 28-day sacrifice (350 and 1,000 mg/kg-day in males, all doses in females) Effects on the liver were reversible by the end of the recovery period; authors consider this effect to be an adaptive rather than toxic response due to the lack of related histopathologic or serum chemistry changes No clinical signs of toxicity and no adverse effects on survival, food consumption, body weight or hematological/serum chemistry values; no gross or microscopic lesions that could be attributed to the test article; no adverse results in functional observation battery or motor activity tests NOAEL = 1,000 mg/kg-day (highest dose tested) LOAEL = Not established	Chengelis, 1997 (as cited in EPA, 2005; NICNAS, 2012)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Lifetime (18-month) dietary bioassay in B6C3F1 mice (50/sex/dose) Doses: 0, 100, 1,000 or 10,000 ppm (0, 13, 130 or 1,300 mg/kg-day for 18 months No adverse effect on mortality, clinical signs, body weight or food consumption Gross lesions/nodules were observed at necropsy (hepatocyte swelling, degeneration, necrosis, vacuole formation and fatty infiltration); however, effects were not dose-related Tumors were sporadic in incidence and not related to test article NOAEL = 1,300 mg/kg-day (10,000 ppm; highest dose tested) LOAEL = Not established	Kurokawa et al., 1984 (as cited in EINECS, 2008; EPA, 2005; NICNAS, 2012)	Reported in a secondary source. Study was not conducted according to OECD guidelines.
Skin Sensitization		**LOW: Based on negative results for skin sensitization in human volunteers and guinea pigs.**		
	Skin Sensitization	Negative, patch test with 10% HBCD in volunteers	EPA, 2005	Reported in a secondary source. Guideline study.
		Negative, guinea pigs	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.
		Negative, mice: Local lymph node assay with 2, 20 or 50% w/v HBCD in DMF	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Positive, guinea pigs Intra-dermal injection and topical application	EINECS, 2008; EPA, 2005; NICNAS, 2012	Reported in a secondary source. Results are questionable; impurities unknown). In addition, the study was an intra-dermal injection study and acetone was used as the vehicle in the dermal challenge phase of the tests, which promotes penetration on shaved skin.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**VERY LOW: HBCD is not an eye irritant in rabbits.**		
	Eye Irritation	Non-irritant, rabbits	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details.
Dermal Irritation		**VERY LOW: HBCD is not a dermal irritant in rabbits or guinea pigs.**		
	Dermal Irritation	Non-irritant, rabbits	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details.
		Non-irritant, guinea pigs	EINECS, 2008	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Endocrine Activity	***In vivo:*** **Thyroid effects were noted following repeated HBCD *in vivo* exposure in rats. Increased TSH levels were reported in F_0 females (14 mg/kg-day) and F_1 females (1,363 mg/kg-day) exposed to HBCD in a two-generation dietary study. In addition, increased size of thyroid follicular cells in F_0 females (141 mg/kg-day), decreased serum FSH levels in F_0 males, increased FSH levels in F_0 females and increased DHT in F_1 males were reported at the highest dose tested (1,008-1,363 mg/kg-day). Increased relative thyroid weights and increased incidence of thyroid follicular cell hypertrophy were reported in dams exposed on gestation day (GD) 10 until postnatal day (PND) 20 at a dose of 1,504.8 mg/kg-day in a dietary study in rats. Offspring developed weak hypothyroidism with increased thyroid weight, increased incidence of thyroid follicular cell hypertrophy, increased FSH levels and decreased T3 concentrations at 1,504.8 mg/kg-day. In this same study, increased thyroid weight and decreased serum T3 concentrations were reported in adult stage male offspring at 146.3 mg/kg-day. Thyroid microfollicular hyperplasia and increased activity of the thyroid epithelium were reported at a dose of 940 mg/kg-day in rats following gavage exposure for 28 days. These effects were attributed to hypermetabolism based on increased thyroid activity, and no pathological findings were noted. Minimal thyroid follicular cell hypertrophy was reported at 1,000 mg/kg-day following a 90-day gavage study in rats. In fish, disruption of thyroid axis (lower circular FT4 and higher FT3; increase in thyroid epithelial cell height) was evident in γ-HBCD-exposed *Oncorhynchus mykiss*. Fish fed a α-HBCD-enriched diet exhibited altered glucuronyltransferase activity and thyroid epithelial cell heights, and fish fed β-HBCD had altered FT4 and FT3 and glucuronyltransferase activity. In contrast, limited potential for endocrine disruption of the thyroid hormonal system was noted in *Platichthys flesus* (flounder) exposed to a technical mixture of HBCD (α-, β- and γ-diastereomers) in sediment and food for 78 days. HBCD alone or in combination with T3 facilitated very fast tail tip regression in tadpoles in an *ex vivo* study.** ***In vitro:*** **HBCD exhibited antiandrogenic, antiprogesteronic and T3-potentiating properties, and a low binding of thyroxine to transthyretin (TTR) in rat pituitary cells and rat pituitary tumor GH3 cells, activated thyroid receptor in the presence of T3 in human cervical carcinoma cells, and is a pregnane X receptor (PXR) agonist in rat and human hepatoma cells. In addition, γ-HBCD is a moderate androgen receptor (AR) and progesterone receptor (PR) antagonist in rat pituitary tumor GH3 cells, while there was no antagonistic activation detected for aryl hydrocarbon receptor (AhR) and estrogen receptor (ER). α-HBCD and γ-HBCD showed T3-enhanced activity in the T-screen assay, and there was no inhibition of estradiol (E2) sulfotransferate in rat pituitary tumor GH3 cells. Xenobiotic-metabolizing enzymes and genes associated with the TH pathway and lipid regulation were noted to be sensitive to HBCD in an *in vitro* study in chicken hepatocytes.**		

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Representative *in vivo* studies		
	28-Day gavage study in Sprague-Dawley rats (10/sex/group) Doses: 0, 1, 2.5 and 5% (0, 940, 2,410 and 4,820 mg/kg--day) Thyroid microfollicular hyperplasia and increased activity of the thyroid epithelium were reported at 1% (940 mg/kg-day); these effects were more marked at 2.5 % (2,410 mg/kg-day), and very marked hyperplastic thyroid tissue with adenomatous proliferation and epithelial hyperactivity was reported at 5% (4,820 mg/kg-day); it is not specified if these effects occurred in the control group Very slight numerical development of the follicles and ripening follicles in the ovaries (4,820 mg/kg-day) Effects on the thyroid were attributed to hypermetabolism as a result of increased thyroid activity, and effects were not pathologic according to the study authors No clinical signs related to treatment or changes in any other organ; no change in clinical chemistry parameters	Zeller and Kirsch, 1969 (as cited in EPA, 2005)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	90-Day gavage study in Crl:CDC(SD)IGS rats (15/sex/group) Doses: 0, 100, 300 and 1,000 mg/kg-day at a dosage volume of 5 mL/kg in corn oil; test article was a composite of three lots of commercial HBCD Minimal thyroid follicular cell hypertrophy (1,000 mg/kg-day); it is not apparent if these changes were related to treatment (authors state that changes may have been a related to reduced serum T4 levels, which is a normal physiological response of healthy organisms acting to maintain serum T4 levels in the normal range) No adverse changes to the estrus cycle or to sperm motility/viability, morphology or number	Chengelis, 2001 (as cited in EPA, 2005)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Two-generation dietary study in Crl:CD(SD) rats (24/sex/group) Doses: 0, 150, 1,500 or 15,000 ppm (10-14, 101-141 or 1,008-1,363 mg/kg-day) Mean daily intake during entire administration: 10.2, 101 and 1,008 mg/kg-day (F_0 males); 14, 141 and 1,363 mg/kg-day (F_0 females); 11.4, 115 and 1,142 mg/kg-day (F1 males); and 14.3, 138 and 1,363 mg/kg-day (F_1 females) Increased TSH (F0 females at ≥150 ppm and $_{F1}$ females at ≥15,000 ppm); decreased serum FSH levels in F_0 males and increased in F_0 females at 15,000 ppm; increased DHT in F_1 males (15,000 ppm); increased incidence of decreased size of thyroid follicular cells in F_0 females (1,500 ppm) No significant differences in serum testosterone, estradiol, progesterone or LH levels Authors conclude that the effect on TSH levels is consistent through dose groups and generations, and is considered an effect of HBCD exposure	Ema et al., 2008 (as cited in EINECS, 2008; NICNAS, 2012)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Dietary study in pregnant Crj:CD rats; Doses: 0, 100, 1,000 or 10,000 ppm (0, 8.1-21.3, 80.7-212.9 or 803.2-2,231.3 mg/kg-day) from gestation day (GD) 10 until postnatal day (PND) 20. Time weighted average (TWA) doses: 0, 14.8, 146.3 or 1,504.8 mg/kg-day Dams: increased relative thyroid weights; tendency for increase in the incidence of thyroid follicular cell hypertrophy at 100 and 1,000 ppm (TWA dose 14.8 and 146 mg/kg-day, respectively); statistically significant at 10,000 ppm (TWA dose 1,504.8 mg/kg-day) Offspring: weak hypothyroidism with increased thyroid weight, increased incidence of thyroid follicular cell hypertrophy, increased TSH concentrations and decreased T3 concentrations at 10,000 ppm (1,504.8 mg/kg-day); increased thyroid weight and decreased serum T3 concentrations when offspring reached adult stage at 1,000 ppm (146.3 mg/kg-day)	Saegusa et al., 2009	Lowest end of maternal exposure range used to determine LOAEL and NOAEL values for maternal and developmental toxicity and thus, hazard. Study does not consider litter effects. Time weighted average (TWA) doses were calculated by multiplying the HBCD intake (mg/kg-day) by the number of inclusive days of exposure for each time point. The sum of each time point for an individual dietary concentration (100, 1,000 and 12,000 ppm) was divided by the total number of inclusive days (33 days) of exposure. Dosing administered from gestation day (GD) 10 to postnatal day (PND) 20 = GDs 10-20: 0, 8.1, 80.7 and 803.2 mg/kg-day; PNDs 1-9: 0, 14.3, 138.7 and 1,404.8 mg/kg-day; PNDs 9-20: 0, 21.3, 212.9 and 2,231.3 mg/kg-day (described in study report).

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In vivo study in *Platichthys flesus* (flounder) exposed to HBCD in sediment and food for 78 days; test substance was a technical mixture of 10.28, 8.72 and 81.01% of α-, β- and γ-diastereomers, respectively; maximum concentration was 446 µg HBCD/g lipid weight (lw) No adverse effects on behavior. No histopathological changes in internal organs including liver, spleen, kidney, gonads and thyroid gland related to HBCD exposure Limited potential for *in vivo* endocrine disruption of the reproductive and thyroid hormonal system	Kupier et al., 2007 (as cited in EINECS, 2008)	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Dietary study in *Oncorhynchus mykiss*, fed either reference diet or three diets enriched with α-, β- or γ-HBCD for 56 days Test concentrations were 0.47 and 0.84 ng/g (α- and γ-HBCD, respectively) Disruption of thyroid axis most evident in γ-HBCD-exposed group (lower circular FT4 and higher FT3; increase in thyroid epithelial cell height) Fish fed the α-HBCD-enriched diet also exhibited altered glucuronyltransferase activity and thyroid epithelial cell heights and the β-HBCD group had altered FT4 and FT3 and glucuronyltransferase activity	Palace et al., 2008	Guideline study. The β-isomer was below the detection limit.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Representative *ex vivo* studies		
	Ex vivo thyroid hormone disruptive study in *Xenopus laevis* tadpoles Doses: 1,000 or 10,000 nM HBCD alone or 20 nM T3 in combination with 10, 100, 1,000 or 10,000 nM HBCD Very fast tail tip regression at 1,000 nM HBCD alone or in combination with T3 during the first 2 days of exposure; no further regression during the rest of the exposure period; no effect on tail regression at doses <1,000 nM Authors conclude that regression was due to cytotoxic activity	Schriks et al., 2006 (as cited in EINECS, 2008)	Reported in a secondary source. Non-guideline study. Not validated according to OECD guidelines and no results from metabolic activation reported.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Representative *in vitro* studies		
	In vitro study using rat pituitary cells to test potential effects of HBCD as an endocrine disruptor Doses (test for T3 potentiating effect): 10-12.5 µM (maximum concentration) for 24 hours in the presence or absence of a reference agonist. Doses (test for potency at act as a thyroid hormone receptor (TR) agonist or antagonist): 1 µM (maximum concentration) for 96 hours in the presence or absence of T3 hormone HBCD exhibited antiandrogenic, antiprogesteronic and T3-potentiating properties *in vitro*, and a low binding to thyroxine binding to TTR	Hamers et al., 2006 (as cited in EINECS, 2008)	Reported in a secondary source. EINECS (2008) states: Study not validated according to OECD guidelines.
	In vitro study using human cervical carcinoma cells HBCD activated thyroid receptor in the presence of T3	Fery et al., 2009	Test substance: HBCD containing 10.3% α, 8.7% β, and 81.0% γ-HBCD.
	In vitro study using rat and human hepatoma cells HBCD is a pregnane-X-receptor (PXR) agonist, which may account for disrupted thyroid activity	Fery et al., 2009	Test substance: HBCD containing 10.3% α, 8.7% β, and 81.0% γ-HBCD.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	In vitro study using rat pituitary tumor GH3 cell line Dose: Maximum concentration of 1 µM in the presence or absence of T3 hormone for 96 hours Moderate AR and PR antagonistic activity was reported for γ-HBCD. Very low or no antagonistic activation was detected for the other two receptors, AhR and ER. α-HBCD and γ-HBCD showed T3-enhanced activity at 1 µM in the T-screen assay No inhibition of E2 sulfotransferase HBCD exhibited antiandrogenic, antiprogesteronic and T3-potentiating properties *in vitro*, and a low binding to TTR	EINECS, 2008; Marvin et al., 2011	Non-guideline study. No results from metabolic activation reported and not validated according to OECD guidelines.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		In vitro study in chicken (*Gallus domesticus)* hepatocytes exposed to nominal concentrations of 0.001-30 µM α-HBCD for 24 or 36 hours Exposure to ≥1 mM resulted in significant upregulation of cytochrome P450 2H1 and CYP3A37 at 24 and 36 hours; significant downregulation of transthyretin, thyroid hormone-responsive spot 14-α and liver fatty acid-binding protein Results indicate that xenobiotic-metabolizing enzymes and genes associated with the TH pathway and lipid regulation are vulnerable to HBCD	Crump et al., 2008	Guideline study.
Immunotoxicity		**HBCD exposure resulted in decreased total number of spleen cells, decreased T-helper and natural killer (NK) cells and decreased NK cell activity in rats.**		
	Immune System Effects	28-Day gavage study in 7-week-old male Wistar rats (5/group) Doses: 0, 0.3, 1, 3, 10, 30, 100 and 200 mg/kg- day in corn oil Decreased total number of cells per spleen, T-helper cells and NK cells; decreased NK cell activity (general decreasing trend, but increased at the high dose)	EINECS, 2008	Reported in a secondary source. Performed according the current OECD guidelines. However, study was not GLP and only limited study details were reported; data based on a small number of animals and only males were tested. No changes in spleen weight or histopathological effects were noted; therefore, the toxicological relevance of these findings is uncertain.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
ECOTOXICITY			
ECOSAR Class	Neutral organics		
Acute Aquatic Toxicity	**VERY HIGH: Based on an EC_{50} of 0.027 mg/L in algae. NES is expected based on physical-chemical properties and other experimental and estimated values for fish, daphnia and algae; however, there is some indication of toxicity to algae at concentrations that are within the range of water solubility.**		
Fish LC_{50}	*Oncorhynchus mykiss* 96-hour LC_{50} >0.0068 mg/L (nominal) or >0.0025 mg/L (mean measured)	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Guideline study. Performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility.
	Lepomis macrochirus 96-hour LC_{50} >100 mg/L (nominal)	EPA, 2005	Reported in a secondary source with limited study details. Value exceeds water solubility.
	Leuciscus idus 96-hour LC_{50} >10,000 mg/L (nominal)	EPA, 2005	Reported in a secondary source with limited study details. Value exceeds water solubility.
	Fish 96-hour LC_{50} = 0.30 mg/L (Estimated) ECOSAR class: Neutral organics	ECOSAR v1.10	NES: The log K_{ow} of 5.6 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Brachydanio rerio exposed to 0, 0.05, 0.1, 0.5 and 1.0 mg L for up to 96 hours. Cell apoptosis, induction of reactive oxygen species (ROS) at 0.1, 0.5 and 1.0 mg/L. Exposure to HBCD results in oxidative stress and may induce apoptosis through involvement of caspases NOEC = 0.05 mg/L LOEC = 0.1 mg/L	Deng et al., 2009	Guideline study. Study details taken from abstract. This study is for a nontraditional endpoint for determining hazard designation. In addition, NOEC and LOEC values are above the limit of water solubility and will not be used to determine a hazard designation. No effects at saturation (NES) are predicted.
Daphnid LC_{50}	*Daphnia magna* 48-hour EC_{50} >0.0068 mg/L (nominal) or >0.0032 mg/L (mean measured)	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility; NES.
	D. magna 48-hour EC_{50} = 146 mg/L (nominal) Nominal test concentrations were 0.01-1,000 mg/L (both below and above the water solubility)	EINECS, 2008	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Value exceeds water solubility.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Daphnia 48-hour LC_{50} = 0.23 mg/L (Estimated) ECOSAR class: Neutral organics	ECOSAR v 1.10	NES: The log K_{ow} of 5.6 for this chemical exceeds the SAR limitation for the log K_{ow} of 5.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	*Skeletonema costatum* 72-hour NOEC >0.01 mg/L (>10 µg HBCD) EC_{50} = 0.027 mg/L (biomass) EC_{50} = 0.052 mg/L (growth rate)	Desjardins et al., 2005; ECHA, 2008	Reported in a secondary source with limited study details.
	Pseudokirchneriella subcapitata 96-hour EC_{50} >0.0068 mg/L (nominal) or >0.0037 mg/L (mean measured)	EPA, 2005; NICNAS, 2012	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. No toxicity at HBCD's limit of water solubility; NES.
	Chlorella sp. 96-hour EC_{50} >1.5 mg/L	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility; NES.
	S. costatum 72-hour EC_{50} >0.0093-0.012 mg/L	EPA, 2005; NICNAS, 2012	Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility; NES.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	S. costatum 96-hour EC_{50} >0.0025 mg/L	ECHA, 2008	Reported in a secondary source with limited study details. The test substance was made up of a composite of HBCD samples from three manufacturers containing 6.0% α-, 8.5% β- and 79.1% γ-diastereomers; total HBCD was 93.6% of test substance. There were no effects at the highest concentration tested.
	S. costatum 72-hour EC_{50} >0.0406 mg/L (40.6 µg HBCD/L) NOEC >0.0406 mg/L (only concentration tested) LOEC = Not identified	Desjardins et al., 2004 (as cited in ECHA, 2008; NICNAS, 2012)	Reported in a secondary source with limited study details; LOECs were not identified. One test concentration at the limit of water solubility; NES.
	Thalassiosira pseudonana 72-hour EC_{50} >0.05–0.37 mg/L	Walsh et al., 1987 (as cited in EPA, 2005; NICNAS)	Reported in a secondary source with limited study details. No toxicity at HBCD's limit of water solubility.
	Scenedesmus subspicatus 96-hour EC_{50} >500 mg/L No effect on growth inhibition	Siebel-Sauer and Bias, 1987 (as cited in EINECS, 2008)	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Value exceeds water solubility.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae 96-hour EC_{50} = 0.29 mg/L (Estimated) ECOSAR class: Neutral organics	ECOSAR v. 1.10	The estimated effect exceeds the water solubility of 0.66 mg/L, but not by 10x as required to be considered NES by ECOSAR. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Chronic Aquatic Toxicity	**VERY HIGH: Based on experimental 21-day LOEC = 0.0056 mg/L and NOEC = 0.0031 mg/L for γ-HBCD in *Daphnia magna*.**		
Fish ChV	*Oncorhynchus mykiss* 88-day NOEC >0.0037 mg/L (γ-HBCD). 27-Day hatching period; 61 days post-hatch showed no effects on hatching success, time to swim-up, larval survival, fry survival or growth	Drotter et al., 2001; EPA, 2005	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP; LOEC and MATC could not be determined due to absence of toxicity, but were considered >0.0037 or 0.0068 mg/L (more than twice γ-HBCD's water solubility). HBCD was not chronically toxic to rainbow trout at concentrations at or above its limit of solubility.
	Fish ChV = 0.043 mg/L (Estimated) ECOSAR class: Neutral organics	ECOSAR v. 1.10	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Chinese rare minnow 14-, 28- and 42-day waterborne HBCD exposure to 0.1-0.5 mg/L Induced hepatic enzymes (as measured by EROD and PROD) Induced oxidative stress in fish brain (as measured by ROS and TBARS) 28-day LOEC = 0.5 mg/L 42-day LOEC = 0.1 mg/L	Zhang et al., 2008	Study details reported in abstract. Values exceed water solubility. This study is for a non-traditional endpoint for determining hazard designation. In addition, LOEC values are above the limit of water solubility and will not be used to determine a hazard designation. A NOEC was not identified.
Daphnid ChV	*D. magna* 21-day life cycle toxicity test. Nominal test concentrations were 0.85, 1.7, 3.4 and 13.6 µg/L; measured test concentrations were 0.87, 1.6, 3.1, 5.6 and 11 µg/L. LOEC = 0.0056 mg/L ([0.0042 mg/L geometric mean]; reduced mean lengths) NOEC = 0.0031 mg/L (γ-HBCD, measured)	Drotter and Kruger, 1998 (as cited in EINECS, 2008; EPA, 2005; NICNAS, 2012)	Reported in a secondary source. Guideline study performed according to current EPA, OECD guidelines and GLP. Within the range of water solubility. The test substance was made up of a composite of HBCD samples from three manufacturers containing 6.0% α-, 8.5% β- and 79.1% γ-diastereomers; total HBCD was 93.6% of test substance. Reduced lengths, dry weight and fewer young observed in daphnia exposed to 0.011 mg/L.
	Daphnia ChV = 0.0.059 mg/L (Estimated) ECOSAR class: Neutral organics	ECOSAR v. 1.10	Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae ChV	Green algae ChV = 0.38 mg/L (Estimated) ECOSAR class: Neutral organics	ECOSAR v. 1.10	The effect level exceeds the water solubility of 0.66 mg/L, but not by 10x as required to be considered NES by ECOSAR. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Earthworm Subchronic Toxicity	*Lumbriculus variegates* 28-day sediment bioassay (spiked and aged sediment) 0.05, 0.5, 5, 50 and 500 mg HBCD/kg dwt (nominal) LOEC = 28.7 mg/kg (rate of emergence) NOEC = 3.2 mg/kg dwt Mean number of eggs in F1 generation was significantly reduced at highest concentration (159 mg/kg dwt)	EINECS, 2008; Oetken et al., 2001	Performed in contrast with OECD Draft Guideline 218, artificial sediment with a coarse grain size (100-2,000 µm) and other carbon sources (stinging-nettle and leaves of alder). EINECS states that the results for total emergence and emergence rate were not considered valid for the purpose of risk assessment due to the large variations in solvent control.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Avian Toxicity	**HBCD exposure produced adverse effects on reproduction in birds. In Japanese quail (*Coturnix coturnix japonica),* dietary exposure of HBCD caused a reduction in hatchability of eggs (125 ppm), reduced shell thickness (>125 ppm), decreased egg weight and an increase in the number of cracked eggs (500 and 1,000 ppm). The NOAEC for reproductive performance in this study was determined to be 5 ppm (0.7 mg/kg bw-day). In a dietary study in American Kestrels (*Falco sparcerius*), HBCD exposure resulted in delayed egg laying, reduced egg size, thinner egg shells, differential weight loss during embryonic development and reduced fertility (concentrations not specified).**		
Reproductive Toxicity to Birds	6-week dietary study in Japanese quails (*Coturnix coturnix japonica*). Doses: 0, 125, 250, 500 or 1,000 ppm of HBCD (a mixture of isomers: α-, 27%; β-, 30%; γ-,43%). Reduction in hatchability at all concentrations tested. Reduction in egg shell thickness at > 125 ppm. Decreased egg weight and egg production rate, increase in cracked eggs at 500 and 1,000 ppm. Additional test conducted for reproductive performance. Doses: 0, 5, 15, 45 or 125 ppm. Reduced survival of chicks at ≥ 15 ppm. NOEC (reproductive performance): 5 ppm (0.7 mg/kg bw-day)	MOEJ, 2009	Limited study details; only abstract is available.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Dietary study in American Kestrels (*Falco sparcerius*) fed HBCD and PBDE Delayed egg laying, smaller eggs, thinner eggshells, differential weight loss during embryonic development and reduced fertility and reproductive success	Fernie et al., 2009	Exposure was to a mixture of HBCD and PBDE. There are currently no DfE criteria to determine a hazard designation for this endpoint.
ENVIRONMENTAL FATE			
Transport	**The transport evaluation for HBCD is based on both estimated and experimental physical and chemical properties. HBCD has been found widespread, in many environmental and ecological samples, even in remote regions such as the Arctic, where concentrations in the atmosphere and top predators are elevated. In the atmosphere, HBCD is expected to exist in both the vapor and particulate phase. Vapor-phase HBCD is expected to have limited potential for photodegradation. Particulate-phase HBCD will be removed from air by wet or dry deposition. Based on the fugacity models incorporating the available experimental property data, HBCD is expected to partition primarily to soil. HBCD is expected to have low mobility in soil based on its estimated K_{oc}. Therefore, leaching of HBCD through soil to groundwater is not expected to be an important transport mechanism. Estimated volatilization half-lives for a model river and model lake indicate that HBCD will have low to moderate potential to volatilize. Volatilization from water surfaces is expected to be attenuated by adsorption to suspended solids and sediment in the water column.**		
Henry's Law Constant – HLC (atm-m^3/mole)	4.6×10^{-5} at 25ºC (Calculated from Measured values)	EPI/Physprop database for CASRN 3194-55-6	Derived from measured vapor pressure (4.7×10^{-7} mm Hg) and water solubility (8.6×10^{-3} mg/L) values.
	6.0×10^{-6} at 25ºC (Estimated)	EPI	Value was obtained from the measured vapor pressure and water solubility.
	α-HBCD: 4.8×10^{-9} β-HBCD: 1.3×10^{-8} γ-HBCD: 3.5×10^{-10} (Calculated from Measured values)	Kuramochi et al., 2010	Value was obtained from the measured vapor pressure (α-HBCD 7.9×10^{-11}; β-HBCD 4.4×10^{-11}; γ-HBCD 6.3×10^{-13}) and water solubility.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	9.1×10^4 (Estimated)	EPI	
	Level III Fugacity Model	Air = 0.4% (Estimated) Water = 6.3% Soil = 54% Sediment = 39.5%	EPI	Values were obtained from the measured vapor pressure, log K_{ow} and water solubility.
Persistence		**HIGH: The persistence designation for HBCD is high. HBCD was considered by the Executive Body of the United Nations Economic Commission for Europe (UNECE) Convention on Long-Range Trans-boundary Air Pollution (LRTAP) to meet the criteria for persistent organic pollutants (POPs) as defined under the POPs protocol. HBCD is persistent in the air, and as such, has been detected in remote regions including the Arctic, and in sediment layers from the 1960s and 1970s through core sampling studies. HBCD is not expected to appreciably degrade under aerobic conditions. Degradation through debromination may occur under anaerobic conditions. Experimental studies indicate no degradation after 28 days in a ready biodegradation test. Aerobic biodegradation data obtained in soil also suggest high persistence. Experimental simulation studies indicate that anaerobic biodegradation of HBCD is possible; however, the removal rate suggests high environmental persistence, and sediment core samples show a significantly slower apparent decrease of HBCD concentrations with time compared to what would be expected based on the half-lives obtained from sediment biodegradation simulation tests. HBCD is not expected to hydrolyze in the environment based on experimental and estimated data. No experimental data were available for the photolysis of HBCD; however, it is not expected to undergo direct photolysis by sunlight as it does not contain chromophores that absorb at wavelengths >290 nm.**		
Water	**Aerobic Biodegradation**	No degradation after 28 days (Measured) OECD Test Guideline 301D	EINECS, 2008; NICNAS, 2012	Values reported in a secondary source. Guideline studies performed according to current EPA, OECD guidelines and GLP.
		Approximately 22% degradation after 56 days; aerobic sludge inherent biodegradation study (Measured) OECD Test Guideline 302B	EINECS, 2008; NICNAS, 2012	

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		87-92% degradation of the three HBCD diastereomers after 60 days under anaerobic conditions using activated sludge (Measured)	NICNAS, 2012	
	Volatilization Half-life for Model River	10 days (Estimated)	EPI	Estimation model was calculated using all applicable measured input values and the Henry's Law constant obtained from the measured vapor pressure and water solubility. It should be noted that this mechanism of HBCD transport should be attenuated by the strong sorption potential of HBCD to suspended material.
	Volatilization Half-life for Model Lake	122 days (Estimated)	EPI	Estimation model was calculated using all applicable measured input values and the Henry's Law constant obtained from the measured vapor pressure and water solubility.
Soil	**Aerobic Biodegradation**	Half-life of γ-HBCD: 63 days at 20°C (Measured) OECD Test Guideline 307	ECHA, 2008; NICNAS, 2012	Value reported in a secondary source. Soil simulation dissipation study using sandy loam soil amended with sewage sludge.
		No degradation after 112 days (Measured) OECD Test Guideline 307	ECHA, 2008; NICNAS, 2012	Reported in a secondary source. Soil simulation dissipation study.
	Anaerobic Biodegradation	Half-life of γ-HBCD: 7 days at 20°C (Measured) OECD Test Guideline 307	EINECS, 2008; NICNAS, 2012	Reported in a secondary source. Soil simulation dissipation study using sandy loam soil amended with sewage sludge.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Half-life: 1.6 days at 37°C (Measured)	EINECS, 2008	Reported in a secondary source. Test substance was a technical HBCD mixture. Performed using sewage sludge in anaerobic conditions.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation	Aerobic sediment half-life: 101 days Anaerobic sediment half-life: 66 days (Measured) OECD Test Guideline 308 α-HBCD: 113 days β-HBCD: 68 days γ-HBCD: 104 days Study reported a stepwise reductive dehalogenation via tetrabromocyclododecene and dibromocyclododecadiene to 1,5,9-cyclododecatriene in aerobic and anaerobic sediment; further degradation beyond 1,5,9-cyclododecatriene was not observed	ECHA, 2008	Reported in a secondary source. Guideline study; provides supporting information concerning the isomer profile of HBCD degradation.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Aerobic sediment half-life: 11 days; 32 days Anaerobic sediment half-life: 2 days (γ-HBCD) (Measured) OECD Test Guideline 308	ECHA, 2008; NICNAS, 2012	Value reported in a secondary source. Guideline study. The test concentration was too low to allow for the quantification of α- and β-diastereomers. No mass balance could be established during the test. The recovery of the test substance varied (33-125%), indicating problems with the extraction method. It is stated that the half-life values obtained from this study may overestimate the degradability of γ-HBCD.
		Degraded by abiotic and biotic processes in soil and aquatic sediment with reported half-lives of 2 days to 2 months (Measured)	Davis et al., 2005, 2006; EPA, 2010	Provides supporting information about HBCD degradation.
		HBCD was detected in sediment layers from the 1960s and 1970s in sediment core studies; sediment layers from the Stockholm archipelago, approximately 30 and 40 years old, were found to contain HBCD in 25-33% of the concentration found in the top layer (approximately 2,004) (Measured)	ECHA, 2008	Non-guideline sediment core studies reported in a secondary source; suggests that degradation half-lives under field conditions may not be as fast as simulation degradation studies indicate.
Air	**Atmospheric Half-life**	1.7 days (Estimated)	EPI	
Reactivity	**Photolysis**	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	The substance does not contain functional groups that would be expected to absorb light at wavelengths >290 nm.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		UV absorbance <240 nm calculated for α, β and γ HBCD diastereomers using time dependent-density functional theory (TD-DFT).	Zhao et al., 2010	HBCD photodegradation and photostereoisomerization trends at wavelengths below 240 nm were predicted. Based on this report, there is potential for degradation of HBCD by UV light, although it is expected to have limited influence on the overall rate of removal.
	Hydrolysis	No degradation after 39 days (Measured)	EINECS, 2008	Reported in a secondary source with limited study details. The measurement was performed on the technical product. The detection limit of 200 ppm may be too high to be reliable.
		Half-life at pH 8: 1.2×10^{10} years Half-life at pH 7: 1.2×10^{11} years (Estimated)	EPI	This result is unreliable because this substance is outside the domain of the EPI HYDROWIN v2.00 estimation as no cyclic structures were in the alkyl halide training set.
			Professional judgment	HBCD is not expected to undergo hydrolysis in the environment due to the lack of functional groups that hydrolyze under environmental conditions.
Environmental Half-Life		>120 days (Estimated)	PBT Profiler; EPI; Professional judgment	Half-life estimated for the predominant compartment (soil), as determined by EPI and the PBT Profiler methodology. This value is consistent with available measured half-lives.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**VERY HIGH: The bioaccumulation designation for HBCD is based on measured BCF values. Available monitoring data demonstrate HBCD being detected in a range of organisms, including higher trophic level organisms.**		
	Fish BCF	BCF = 8,974 (Measured) *Oncorhynchus mykiss* (whole fish) at a nominal concentration of 3.4 µg HBCD/L for 70 days long (25-day uptake, 35-day depuration); nominal concentrations based on γ-isomer The three stereoisomers of HBCD were present in *O. mykiss* in rough approximation to that of the commercial product used as test article	Drottar and Kruger, 2000; EINECS, 2008; EPA, 2005; NICNAS, 2012	Guideline study performed according to current EPA, OECD guidelines and GLP.
		BCF = 18,100 (Measured) (steady-state, log BCF 4.26) in *Pimephales promelas* at a mean water concentration of 6.2 µg HBCD/L for 32 days	EINECS, 2008; Veith et al., 1979	Non-guideline study that was conducted before the implementation of standardized test procedures for BCF.
	Fish BAF	4,100 (Estimated for 3194-55-6) 350,000 (Estimated for 25637-99-4)	EPI	These estimated results are from the BCFBAF v3.01 Arnot-Gobas method, reporting the upper trophic value with an entered measured Log K_{OW} value of 5.6.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
		Juvenile rainbow trout (*O. mykiss*) were exposed to three HBCD isomers through their diet for 56 days, followed by 112 days of untreated food Steady state was not reached after 56 days; muscle tissue was sampled throughout the study α-HBCD: 9.2 β-HBCD: 4.3 γ-HBCD: 7.2	Law, 2006; NICNAS, 2012	The secondary source reported these calculated results as BAF values; however, the original source refers to these as BMF values. Despite the difference in nomenclature, these values from non-guideline studies demonstrate that HBCD isomers bioaccumulate in fish through dietary exposure.
	Mammalian BAF	90-Day gavage study in Crl:CD(SD)IGS BR rats (20/sex) Doses: 0 and 1,000 mg technical-grade HBCD/kg/day at a dosage volume of 5 mL/kg for 90 days (Measured) Relative BAF α-HBCD: 99 Relative BAF β-HBCD: 11 Relative BAF γ-HBCD: 1	EINECS, 2008	Values were obtained from a secondary source provide supporting information concerning the isomer profile of HBCD bioaccumulation.
	Earthworm BAF	BAF HBCD: 0.03-0.08 wwt/wwt (Measured) A 28-day study in earthworms exposed to concentrations HBCD ranging from 78.5 to 5,000 mg/kg soil (dwt) BAF α-HBCD: 0.3-0.8 dwt/wwt BAF β-HBCD: 0.01-0.04 dwt/wwt BAF γ-HBCD: 0.005-0.02 dwt/wwt	EINECS, 2008; NICNAS, 2012	Values were obtained from a secondary source provide supporting information concerning the isomer profile of HBCD bioaccumulation.

Hexabromocyclododecane (HBCD) CASRN 25637-99-4; 3194-55-6				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Metabolism in Fish	Metabolite formation was studied in juvenile rainbow trout (*O. mykiss*) liver and muscle Bioisomerization: Fish exposed to the β-isomer resulted in α-isomer and γ-isomer Fish exposed to the α-isomer resulted in no β-isomer and a small amount of γ-isomer Fish exposed to the γ-isomer resulted in a linear increase in the α-isomer over the first 14 days of depuration and this isomer was still found after 112 days depuration; no β-isomer was found after 112 days depuration	NICNAS, 2012	Values were obtained from a secondary source and provide species-specific isomer profile information.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		Detected in lake and river sediment, indoor dust, Arctic atmospheric air, deposition samples, European surface waters, point source air, urban air and marine sediment (ECHA, 2008; EINECS, 2008; HSDB, 2011b; NICNAS, 2012; La Guardia et al., 2012).		
Ecological Biomonitoring		Detected in the eggs, liver and blood of Arctic marine birds, Baltic Sea guillemot eggs, Arctic sea ice amphipods, polar cod, skipjack tuna, polar bear adipose tissue, harbor seal blubber, ringed seal blubber, fish and marine mammals in Western Europe, the Baltic Sea and Western Scheldt, U.K. harbor porpoise, plankton, mussels, peregrine falcons in Sweden, Sparrow hawk, Atlantic puffin, Atlantic white sided dolphin, bottle nose dolphin, bull shark, Grey seal, sea lion, Narwhal, bivalve, gastropod, beluga and ring-billed gulls from the St. Lawrence River, Canada (ECHA, 2008, EINECS, 2008, EPA, 2010, NICNAS, 2012, Gentes et al., 2012; La Guardia et al., 2012).		
Human Biomonitoring		Detected in breast milk, blood plasma and adipose tissue. This chemical was not included in the NHANES biomonitoring report (CDC, 2011; ECHA, 2008; HSDB, 2011b; Marvin et al., 2011; NICNAS, 2012).		

Table 1. Summary of benchmark dose model results for decreased serum T3 levels in adult stage (PNW 11) male offspring from Sprague-Dawley rats exposed to HBCD in the diet from gestation day (GD) 10 – postnatal day (PND) 20

Model	Test for significant difference *p*-value[a]	Variance *p*-value[b]	Means *chi-square* *p*-value[b]	Scaled residuals of interest[c]	AIC	$BMD_{RD10\%}$ (mg/kg-day)	$BMDL_{RD10\%}$ (mg/kg-day)
All doses included							
Constant variance							
Exponential	NA						
Hill[e]	0.06	0.77	NA	0.000000188 / -0.28	-178.58	18.67	7.11
Linear[d]	0.06	0.77	0.02	0.20 / HD	-174.60	2376.16	1189.99
Polynomial (2-degree)[d]	0.06	0.77	0.02	0.20 / HD	-174.60	2376.16	1189.99
Polynomial (3-degree)[d]	0.06	0.77	0.02	0.20 / HD	-174.60	2376.16	1189.99
Power[e]	0.06	0.77	0.02	0.20 / HD	-174.60	2376.16	1189.99
Highest dose dropped							
Constant variance							
Exponential (model 2)	**0.05**	**0.57**	**0.38**	**-0.65 / 0.07**	**-134.64**	**119.68**	**73.53**
Exponential (model 3)	0.05	0.57	0.38	-0.65 / 0.07	-134.64	119.68	73.53
Exponential (model 4)	0.05	0.57	NA	4.38E -08 / 2.22E-08	-133.42	39.57	9.73
Hill[e]	NA						
Linear[d]	0.05	0.57	0.37	-0.66 / 0.07	-134.63	120.98	75.95
Polynomial (2-degree)[d]	0.05	0.57	0.37	-0.66 / 0.07	-134.63	120.98	75.95
Power[e]	**0.05**	**0.57**	**0.37**	**-0.66 / 0.07**	**-134.63**	**120.98**	**75.95**

Data from Saegusa et al. 2009

AIC = Akaike Information Criterion; BMD = maximum likelihood estimate of the dose associated with the selected benchmark response; BMDL = 95% lower confidence limit on the BMD; HD = BMD value is higher than the highest dose tested; therefore, only the residual just below the BMD is presented; NA = Model failed to generate; SD = standard deviation

[a]Values >0.05 fail to meet conventional goodness-of-fit criteria.

[b]Values <0.10 fail to meet conventional goodness-of-fit criteria.

[c]Scaled residuals at doses immediately below and immediately above the benchmark dose.

[d]Coefficients restricted to be negative.

[e]Power restricted to ≥1.

The test for significant difference provided a marginal fit to the data for changes in serum T3 levels in rats. The continuous models with constant variance assumed did provide adequate fits to the variance model; however none of the models provided an adequate fit to the means. In an attempt to achieve an adequately fit model, the highest dose was dropped from the dataset and reapplied to the continuous models with constant variance assumed. After dropping the highest dose, all models (linear, polynomial, power, and exponential), with the exception of the Hill model, provided adequate fits to both the variance and the means. Among the fit models, the BMDLs differed by less than 3-fold, so the model with the lowest AIC was selected (exponential model). BMDs and BMDLs associated with a change of one standard deviation were calculated to be 119.68 and 73.53 mg/kg-day, respectively.

Fit of exponential model (model 2) to data for decreased serum T3 levels in adult stage (PNW 11) male offspring from Sprague-Dawley rats exposed to HBCD in the diet from gestation day (GD) 10 – postnatal day (PND) 20

Highest Dose Dropped

The BMD and BMDL indicated are associated with a 1 standard deviation change from the control and are in units of mg/kg day

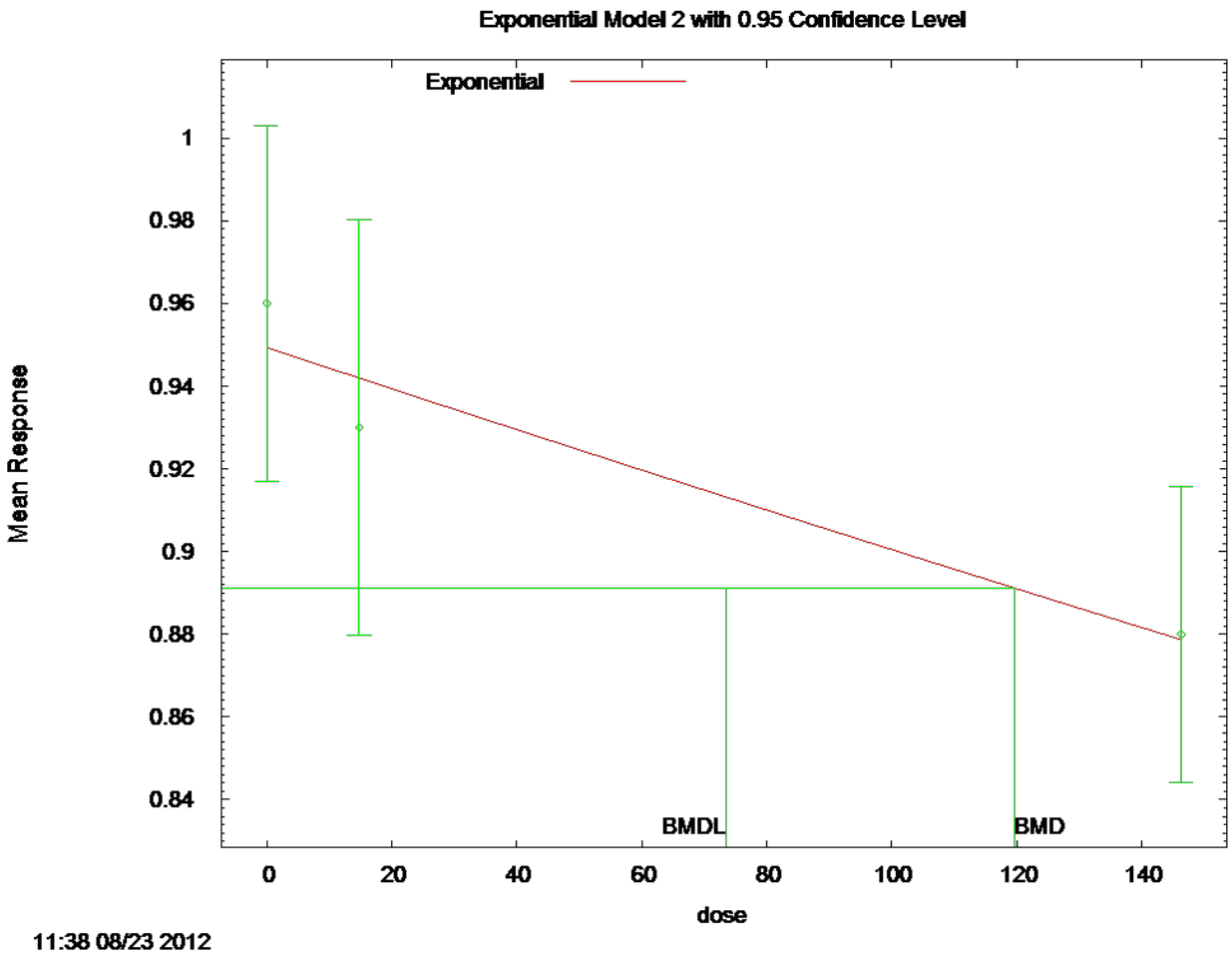


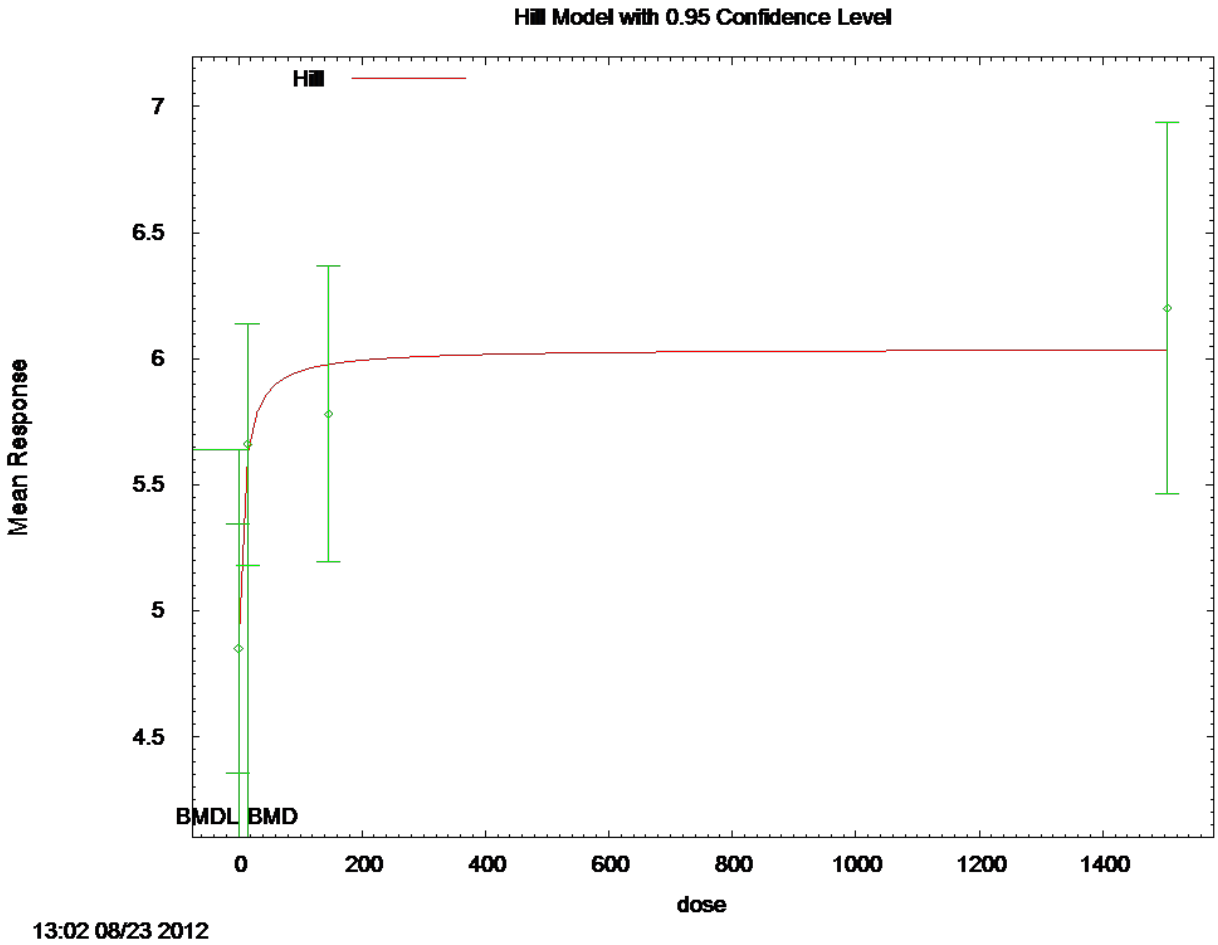
Table 2. Summary of benchmark dose model results for increased relative thyroid weight in adult stage (PNW 11) male offspring from Sprague-Dawley rats exposed to HBCD in the diet from gestation day (GD) 10 – postnatal day (PND) 20

Model	Test for significant difference *p*-value[a]	Variance *p*-value[b]	Means *chi-square* *p*-value[b]	Scaled residuals of interest[c]	AIC	$BMD_{RD10\%}$ (mg/kg-day)	$BMDL_{RD10\%}$ (mg/kg-day)
Constant variance							
Exponential (model 2)	0.01	0.48	0.03	-0.12 / HD	32.47	1518.54	960.56
Exponential (model 3)	0.01	0.48	0.03	-0.12 / HD	32.47	1518.54	960.56
Exponential (model 4)	0.01	0.48	0.23	-0.00004 / 0.00014	28.89	14.01	0.03
Exponential (model 5)	0.01	0.48	0.23	-0.00004 / 0.00014	28.89	14.01	0.04
Hill[e]	**0.01**	**0.48**	**0.29**	**0.16 / -0.80**	**28.57**	**15.85**	**0.00005**
Linear[d]	0.01	0.48	0.03	-0.12 / HD	32.42	1505.30	913.61
Polynomial (2-degree)[d]	0.01	0.48	0.03	-0.12 / HD	32.42	1505.30	913.61
Polynomial (3-degree)[d]	0.01	0.48	0.03	-0.12 / HD	32.42	1505.30	913.61
Power[e]	0.01	0.48	0.03	-0.12 / HD	32.42	1505.30	913.61

Data from Saegusa et al. 2009
AIC = Akaike Information Criterion; BMD = maximum likelihood estimate of the dose associated with the selected benchmark response; BMDL = 95% lower confidence limit on the BMD; HD = BMD value is higher than the highest dose tested; therefore, only the residual just below the BMD is presented; NA = Model failed to generate; SD = standard deviation
[a]Values >0.05 fail to meet conventional goodness-of-fit criteria.
[b]Values <0.10 fail to meet conventional goodness-of-fit criteria.
[c]Scaled residuals at doses immediately below and immediately above the benchmark dose.
[d]Coefficients restricted to be positive.
[e]Power restricted to ≥1.
Models were fit to the data for changes in relative thyroid weight in rats. The continuous models with constant variance assumed did provide adequate fits to the variance model. Only the exponential (models 4 and 5) and Hill models provided an adequate fit to the means. Among the fit models, the BMDLs differed by less than 2- to 3-fold, so the model with the lowest AIC was selected (Hill model). BMDs and BMDLs associated with a change of one standard deviation were calculated to be 15.85 and 0.00005 mg/kg-day, respectively.
The LOAEL for this endpoint was determined to be 146.3 mg/kg-day with a NOAEL of 14.8 mg/kg-day. The BMDL of 0.00005 mg/kg-day, as well as the BMDLs from the exponential (models 4 and 5) models fall below the observed NOAEL for this endpoint, and do not appear to be valid.

Fit of Hill model to data for increased relative thyroid weight in adult stage (PNW 11) male offspring from Sprague-Dawley rats exposed to HBCD in the diet from gestation day (GD) 10 – postnatal day (PND) 20

The BMD and BMDL indicated are associated with a 1 standard deviation change from the control and are in units of mg/kg day



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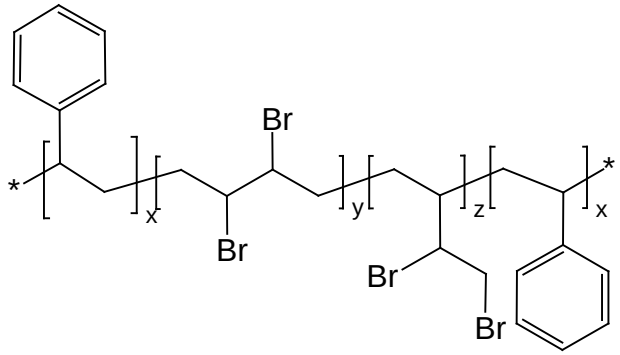
Butadiene styrene brominated copolymer

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH*) were assigned using values from predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

d This hazard designation would be assigned MODERATE for a potential for lung overloading if >5% of the particles are in the respirable range as a result of dust forming operations
¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
Butadiene styrene brominated copolymer¥	1195978-93-8	**L**	***L***	**L**	**L**	**L**	***L***	**L**[d]	**L**		**M**	**L**	***L***	***L***	***VH***	***L***

Butadiene styrene brominated copolymer



Representative structure

CASRN: 1195978-93-8

MW: 60,000-160,000;
≤0.1% <1,000;
≤0.1% <500

MF: $(C_8H_9)_x(C_4H_6Br_2)_y(C_4H_6Br_2)_z$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: This polymer with MW >1,000 and minimal low MW components is not amenable to SMILES notation.

Synonyms: Benzene, ethenyl-, polymer with 1,3-butadiene, brominated (CA Index Name for CASRN 1195978-93-8); Block copolymer of polystyrene and brominated polybutadiene; polymeric FR

Trade Names: Emerald Innovation™ 3000; FR122P

Chemical Considerations: This alternative is a high MW polymer. It was assessed using polymer assessment criteria as described in the literature (Boethling and Nabholz, 1997). The hazard designations shown in the table for this alternative are based upon high MW formulations of the polymer, where all components have a MW >1,000. Future formulations may contain lower MW oligomers or impurities that have the potential to be persistent, bio-accumulative, and toxic (PBT) and are not represented in the hazard designations presented.

This substance is subject to a Significant New Use Rule (SNUR) that was finalized in June 2013 (78 Federal Register 38210). Manufacture (or import) of the polymer requires notification to EPA except in these cases: (1) the MW of the polymer is in the range of 1,000 to 10,000 daltons, or (2) the MW of the polymer is ≥10,000 daltons and less than 5 percent of the particles are in the respirable range of 10 microns or less (EPA, 2013).

Polymeric: Yes **Oligomers:** The average MW of this polymer ranges from 60,000 to 160,000 daltons with oligomers below 500 or 1,000 expected in negligible amounts.	
Metabolites, Degradates and Transformation Products: None identified.	
Analog: No analogs **Endpoint(s) using analog values:** Not applicable	**Structure:** Not applicable
Structural Alerts: None identified	
Risk Phrases: Not classified by Annex VI Regulation (EC) No. 1272/2008 (ESIS, 2011)	
Hazard and Risk Assessments: None identified	

Butadiene styrene brominated copolymer CASRN 1195978-93-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)			No data located.
Boiling Point (°C)	>300 (Estimated)	Professional judgment	Cutoff value used for large, high MW solid.
Vapor Pressure (mm Hg)	$<10^{-8}$ (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large, high MW polymers according to polymer assessment literature.
Water Solubility (mg/L)	No dissolved organic carbon (DOC) was detected in water at pH 2, 7 and 9 at 20°C and pH 7 at 37°C after 24 hours according to test guideline OECD 120 with 0.05 and 0.5 g samples (Measured)	Dow, 2005c	OECD test guideline 120 is for solid polymers for which the Water Solubility OECD 105 test is not applicable. For OECD 120, the solution/extraction behavior of the polymer in water at a range of pH values is analyzed.
	$<10^{-3}$ (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large, high MW non-ionic polymers according to polymer assessment literature.

Butadiene styrene brominated copolymer CASRN 1195978-93-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Log K_{ow}			No data located; polymers with a MW >1,000 are outside the domain of the available estimation methods.
	Approximately 2 (Measured) According to Guideline OECD 117; calculated for residual solvent from an acute invertebrate toxicity study water accommodated fraction (WAF) sample.	Dow, 2007a; Dow, 2012	Inadequate, the log K_{OW} is not consistent with the structure of the material and does not represent the polymeric substance. The sample is from an acute invertebrate toxicity study WAF; polymeric components not found in the WAF were not evaluated. Additionally, this study did not definitively identify the peak detected from the WAF using OECD 117 "Partition Coefficient (N-octanol/water), High Performance Liquid Chromatography (HPLC) Method". Separate analysis of WAF identified the impurities to be solvent present in the sample (i.e. 1,2-dichloroethane).
Flammability (Flash Point)	Nonflammable (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis	DfE assessment methodology indicates that chemicals that contain both halogens and aromatic rings have the potential to form compounds potentially hazardous compounds under high temperature conditions (Estimated)	Professional judgment	Based on analysis of the chemical structure.

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
pH		Not applicable	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a		Not applicable	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**There is no absorption expected for any route of exposure. This polymer is large, with a MW >1,000. It is expected to have limited bioavailability and is therefore not expected to be readily absorbed, distributed or metabolized in the body.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	No absorption expected for any route of exposure (Estimated)	Professional judgment	Estimated based on professional judgment.
Acute Mammalian Toxicity		**LOW: Based on experimental LD_{50} values >2,000 mg/kg. This polymer is also expected to have limited bioavailability and is therefore of low potential for acute mammalian toxicity.**		
Acute Lethality	**Oral**	Oral, rat LD_{50} >2,000 mg/kg in Up and Down Procedure.	Dow, 2007e	Sufficient study details provided.
		Oral, mouse LD_{50} >5,000 mg/kg	Dow, 2005a	Sufficient study details provided.
		Oral, rat LD_{50} >2,000 mg/kg in Up and Down Procedure.	Dow, 2007e	Sufficient study details provided.
	Dermal	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
	Inhalation			
Carcinogenicity		**LOW: This polymer is large, with a MW >1,000. It is expected to have few to no residual monomers. Additionally, it is not expected to have crosslinking, swellability, dispersability, reactive functional groups, potential for inhalation or hindered amine groups. This chemical therefore has a low potential for carcinogenicity. No experimental data located.**		
	OncoLogic Results			No data located.

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Carcinogenicity (Rat and Mouse)	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
	Combined Chronic Toxicity/Carcinogenicity			
Genotoxicity		**LOW: This compound did not induce gene mutations in bacteria or cause chromosomal aberrations in mammalian cells *in vitro*. In addition, this polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for genotoxicity.**		
	Gene Mutation *in vitro*	Negative in Ames assay in *S. typhimurium* TA98, TA100, TA1535, TA1537, and in *E. coli* WP2*uvr*A in the presence of metabolic activation	Dow, 2005b	Sufficient study details and supporting data provided.
	Gene Mutation *in vivo*	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
	Chromosomal Aberrations *in vitro*	Negative in rat lymphocyte chromosomal aberration test (RLCAT)	Dow, 2006	Sufficient study details and supporting data provided.
	Chromosomal Aberrations *in vivo*	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
	DNA Damage and Repair			No data located.
	Other			No data located.
Reproductive Effects		**LOW: Available experimental data indicate a Low hazard designation. In addition, this polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for reproductive effects.**		

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		DATA	REFERENCE	DATA QUALITY
	Reproduction/ Developmental Toxicity Screen	No reproductive effects were observed in combined repeated dose toxicity study (28-day) with reproductive/developmental toxicity screening test in Crl:CD (SD) rats orally exposed to 0, 100, 300, or 1,000 mg/kg-day via gavage. NOAEL >1,000 mg/kg-day (highest dose tested)	Dow, 2007f	Sufficient study details and supporting data provided; effects on reproductive and developmental functions including organ weights, histopathological examinations of tissues, litter size, pup survival, sex, body weight, and the presence of gross external abnormalities were evaluated; conducted according to OECD guidelines.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
	Reproduction and Fertility Effects			

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**LOW: Available experimental data also indicate a Low hazard designation. In addition, this polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for developmental effects.**		
	Reproduction/ Developmental Toxicity Screen	No developmental effects were observed in combined repeated dose toxicity study (28-day) with reproductive/developmental toxicity screening test in Crl:CD (SD) rats orally exposed to 0, 100, 300, or 1,000 mg/kg-day via gavage. Developmental NOAEL >1,000 mg/kg-day (highest dose tested)	Dow, 2007f	Sufficient study details and supporting data provided; effects on reproductive and developmental functions including organ weights, histopathological examinations of tissues, litter size, pup survival, sex, body weight, and the presence of gross external abnormalities were evaluated; conducted according to OECD guidelines.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
	Prenatal Development			
	Postnatal Development			

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**LOW: This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for neurotoxicity. There were no neurological effects reported in a 28-day repeated dose toxicity study in rats at doses as high as 1,000 mg/kg-day.**		
	Neurotoxicity Screening Battery (Adult)	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
		There were no neurological effects observed in a combined repeated dose toxicity study (28-day) with reproductive/ developmental toxicity screening test in Crl:CD (SD) rats orally exposed to 0, 100, 300, or 1,000 mg/kg-day via gavage. NOAEL >1,000 mg/kg-day (highest dose tested)	Dow, 2007f	Sufficient study details and supporting data provided; effects on neurological functions including sensory evaluation, rectal temperature, grip performance, and motor activity were evaluated; conducted according to OECD guidelines.
Repeated Dose Effects		**LOW: Based on an experimental NOAEL >1,000 mg/kg-day in rats exposed via gavage for 28 days. This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; however, because the number average molecular weight (MW_n) is >10,000, there is the possibility of lung overloading in dust forming conditions.**		
		This MW_n for this polymer is >10,000; potential for irreversible lung damage as a result of lung overloading (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
		No adverse effects were observed in a combined repeated dose toxicity study (28-day) with reproductive/developmental toxicity screening test in Crl:CD (SD) rats orally exposed to 0, 100, 300, or 1,000 mg/kg-day via gavage. NOAEL >1,000 mg/kg-day (highest dose tested)	Dow, 2007f	Sufficient study details and supporting data provided; conducted according to OECD guidelines.

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: This polymer did not cause skin sensitization in a guideline study.**		
	Skin Sensitization	Does not cause skin sensitization in guinea pig by Buehler test	Dow, 2007b	Sufficient study details and supporting data provided. Conducted according to OECD Test Guideline 406
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**MODERATE: This polymer is mildly irritating to rabbit eyes, with effects clearing within 72 hours post instillation.**		
	Eye Irritation	Non-irritating (species not specified)	Dow, 2011	Limited study details and no supporting data provided.
		Mildly irritating, rabbits Single instillation of 20 mg of the test substance caused iritis and conjunctivitis, clearing within 72 hours.	Dow, 2007c	Sufficient study details provided; study conducted according to OECD guidelines; evaluated by the Draize method; irritations may have been due to mechanical action (scratching) due to the 20 mg instillation of the test substance particles.
Dermal Irritation		**LOW: This polymer is slightly irritating to the skin of rabbits.**		
	Dermal Irritation	Slightly irritating in rabbits according to OECD Test Guideline 404; caused slight erythema that cleared within 24 hours	Dow, 2007d	Sufficient study details and supporting data provided.
Endocrine Activity		**This polymer is large, with a MW >1,000. It is not expected to have endocrine activity due to its limited bioavailability and inability to be readily metabolized in the body.**		
		Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
Immunotoxicity		**This polymer is large, with a MW >1,000. It is expected to have limited bioavailability; therefore, it has low potential for immunotoxicity.**		

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Immune System Effects	Limited bioavailability expected (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Based on polymer assessment literature.
ECOTOXICITY				
ECOSAR Class		Not applicable		
Acute Aquatic Toxicity		**LOW: Non-ionic polymers with MWs >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to display no effects at saturation (NES). These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Guidance for the assessment of aquatic toxicity hazard results in a Low hazard designation for those materials that display NES. Experimental data for *Daphnia magna* indicate NES with EC_{50} values > 1,000 mg/L; these reported values exceed the compound's water solubility by several orders of magnitude.**		
Fish LC_{50}		NES	Professional judgment	The large MW, limited bioavailability and low water solubility suggest that there will be NES.

Butadiene styrene brominated copolymer CASRN 1195978-93-8			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	*Daphnia magna* 48-hour EL_{50} > 1,000 mg/L. EL_{50} is the effect (immobility) loading rate resulting in 50% immobility; 24-hour EL_{50} > 1,000 mg/L; 48-hour no-observed-effect loading rate (NOELR) < 1,000 mg/L (Experimental)	Dow, 2007a	Sufficient study details provided; study conducted according to OECD Test Guideline 202. The reported value was determined using a water accommodated fraction (WAF) at a loading rate of 1,000 mg (only concentration tested); the toxicity values were determined based on the nominal loading rate used to prepare the WAF solution. As a result, the reported value exceeds this material's water solubility; immobility was reported in 10% (3/30) daphnids at the test dose (1,000 mg/L) following 24- and 48- hours of exposure, therefore the NOELR is determined to be at some concentration less than 1,000 mg/L. Subsequent evaluation determined that the WAF contained solvent impurities
	NES	Professional judgment	The large MW, limited bioavailability and low water solubility suggest that there will be NES.
Green Algae EC_{50}	NES	Professional judgment	The large MW, limited bioavailability and low water solubility suggest that there will be NES.
Chronic Aquatic Toxicity	**LOW: Non-ionic polymers with a MW >1,000 that do not contain reactive functional groups and are comprised of minimal low MW oligomers are estimated to display NES. These polymers display NES because the amount dissolved in water is not anticipated to reach a concentration at which adverse effects may be expressed. Guidance for the assessment of aquatic toxicity hazard results in a low hazard categorization for those materials that display NES.**		

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Fish ChV		NES	Professional judgment	The large MW, limited bioavailability and low water solubility suggest that there will be NES.
Daphnid ChV		NES	Professional judgment	The large MW, limited bioavailability and low water solubility suggest that there will be NES.
Green Algae ChV		NES	Professional judgment	The large MW, limited bioavailability and low water solubility suggest that there will be NES.
ENVIRONMENTAL FATE				
Transport		**The negligible water solubility and estimated negligible vapor pressure indicate that this polymer is anticipated to partition predominantly to soil and sediment. The estimated Henry's Law constant of <10^{-8} atm-m^3/mole indicates that it is not expected to volatilize from water to the atmosphere. The estimated K_{oc} of >30,000 indicates that it is not anticipated to migrate from soil into groundwater and that it has the potential to adsorb to sediment.**		
	Henry's Law Constant (atm-m^3/mole)	<10^{-8} (Estimated)	Professional judgment; Boethling and Nabholz, 1997	High MW polymers are expected to have low vapor pressure and are not expected to undergo volatilization according to polymer assessment literature.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value used for large, high MW polymers. High MW polymers are expected to adsorb strongly to soil and sediment according to polymer assessment literature.
	Level III Fugacity Model			No data located.

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Persistence		**VERY HIGH: This polymer is large, with a MW >1,000. It has negligible water solubility and is expected to have poor bioavailability to microorganisms, indicating that neither biodegradation nor hydrolysis are expected to be important removal processes in the environment. Additionally, experimental guideline studies did not detect anaerobic biodegradation of this polymer after 62 days or degradation by hydrolysis after five days at pH 1.2 to 9. Although debromination by photodegradation of polybrominated benzenes has been observed, this process is not anticipated to lead to ultimate degradation of the material; also, limited debromination is not likely to significantly alter the environmental properties of this material. As a result, a half-life for this high MW polymer of >180 days leads to a potential for Very High persistence.**		
Water	**Aerobic Biodegradation**	Recalcitrant (Estimated)	Professional judgment; Boethling and Nabholz, 1997	High MW synthetic polymers are expected to be non-biodegradable according to polymer assessment literature.
	Volatilization Half-life for Model River	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	Professional judgment	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**			No data located.
	Anaerobic Biodegradation	Anaerobic Biodegradation OECD 311 study exhibited no biodegradation after 62 days (Measured)	Dow, 2009a	Guideline study.
	Soil Biodegradation with Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**			No data located.

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reactivity	**Photolysis**	Photodegradation was detected in studies using the bulk polymer and the polymer in foam; 9,600 ppm water extractable bromide was detected from 0.022 g of bulk polymer samples by IC-MS after 30 days of light exposure from a Xenon arc lamp with a UV glass filter limiting wavelengths below 290 nm at 28-39°C (Measured)	Dow, 2007h; Dow, 2009c	Bromine substituents may be susceptible to photolysis in the environment; however, this is expected to be a relatively slow process for a high MW brominated polymer and is not anticipated to result in the ultimate degradation of this substance.
	Hydrolysis	Not susceptible to hydrolysis according to OECD 111 based on average DOC values of: 1.76 ± 0.51 mg/L at pH 1.2; 0.81 ± 0.30 mg/L at pH 4; 1.25 ± 0.35 mg/L at pH 7; 1.33 ± 0.40 mg/L at pH 9 obtained from 914 ± 112 mg/L of sample at 49.9 °C for 5 days (Measured)	Dow, 2007g	Guideline study.
	Other	This polymer is stable in PEG400 for 21 days; 2.5-250 mg/mL samples analyzed by HPLC/RI (Measured)	Dow, 2007i	This study demonstrates the stability of this compound in PEG400.
Environmental Half-Life		>180 days (Estimated)	Professional judgment	The substance is a high MW synthetic polymer and is not anticipated to be assimilated by microorganisms. Therefore, biodegradation is not expected to be an important removal process. It is also not expected to undergo removal by other degradative processes under environmental conditions.

Butadiene styrene brominated copolymer CASRN 1195978-93-8				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**LOW: Due to the large size and limited bioavailability of the high MW brominated polymer, it is of low potential for bioconcentration or bioaccumulation.**		
	Fish BCF	<100 (Estimated)	Professional judgment; Boethling and Nabholz, 1997	Cutoff value for large, high MW, insoluble polymers according to polymer assessment literature.
	BAF			No data located.
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

Boethling RS, Nabholz JV (1997) Environmental assessment of polymers under the U.S. Toxic Substances Control Act. Washington, DC: U.S. Environmental Protection Agency.

CDC (Centers for Disease Control and Prevention). *Fourth National Report on Human Exposure to Environmental Chemicals, Updated Tables*. Department of Health and Human Services.
2011. http://www.cdc.gov/exposurereport/pdf/FourthReport_UpdatedTables_Feb2012.pdf (accessed on September 14, 2012).

Dow. The Dow Chemical Company. Acute oral toxicity screen in mice. PMN number P10-0476. **2005a**.

Dow. EH&S data summary for polymeric flame retardant (polymeric FR) issued by the Dow Chemical Company. Dow Chemical Company. **2012**.

Dow. The Dow Chemical Company. Charles, G; M; Kleinert, K. Salmonella/E. coli reverse mutation screening assay for [confidential substance][17] with mammalian S-9 activation. PMN number P10-0476. **2005b**.

Dow. The Dow Chemical Company. Charles, G; Schisler, M; Kleinert, K. Evaluation of the alcohol and aqueous extracts of [confidential substance][1] in an in vitro chromosomal aberration assay utilizing rat lymphocytes. PMN number P10-0476. **2006**.

Dow. The Dow Chemical Company. Marino, T; Hales, C; Najar J. An acute toxicity study with the daphnid, Daphnia magna. PMN number P10-0476. **2007a**.

Dow. The Dow Chemical Company. Dermal sensitization study in guinea pigs (Buehler method). PMN number P10-0476. **2007b**.

Dow. The Dow Chemical Company. Primary eye irritation study in rabbits. PMN number P10-0476. **2007c**.

Dow. The Dow Chemical Company. Primary skin irritation study in rabbits. PMN number P10-0476. **2007d**.

Dow. The Dow Chemical Company. Acute oral toxicity up and down procedure in rats. PMN number P10-0476. **2007e**.

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[17] At time of submission of study report, the test substance name was claimed confidential. At notice of commencement (NOC) the confidentiality claim on the chemical identification was retracted.

Dow. The Dow Chemical Company. Yano, B; Zablotny, C; Murray, J. A combined repeated dose toxicity study with the reproduction/developmental toxicity screening test in CRL:CD (SD) rats. PMN number P10-0476. **2007f**.

Dow. The Dow Chemical Company. Determination of Hydrolysis Rate Following OECD 111 Guidelines. PMN number P10-0476. **2007g**.

Dow. The Dow Chemical Company. Evaluation of biodegradability in Anaerobic Digester Sludge According to OECD Guideline 311. PMN number P10-0476. **2009a**.

Dow. The Dow Chemical Company. Evaluation of biodegradability in Anaerobic Digester Sludge According to OECD Guideline 311. PMN number P10-0476. **2009b**.

Dow. The Dow Chemical Company. Exposure of Polymer Samples to Artificial Sunlight Irradiation. PMN number P10-0476. **2007h.**

Dow. The Dow Chemical Company. Exposure of Polystyrene Foam Containing [Confidential substance] polymer to Artificial Sunlight Irradiation: Evaluation of [Confidential substance] Stability. PMN number P10-0476. **2009c**.

Dow. The Dow Chemical Company. Solution/Extraction behavior in Water following the OECD 120 Guideline. PMN number P10-0476. **2005c**.

Dow. The Dow Chemical Company. Stability study. PMN number P10-0476. **2007i**.

Dow. The Dow Chemical Company. Strategic Approach Towards Developing More Environmentally Sustainable Flame Retardants. [Presentation] **2011**.

EPA (U.S. Environmental Protection Agency). Significant New Use Rules on Certain Chemical Substances. 78 FR 38210-38223. **2013**. http://www.gpo.gov/fdsys/pkg/FR-2013-06-26/pdf/2013-15032.pdf (accessed on April 8, 2014).

ESIS (European chemical Substances Information System). Classification, Labeling and Packaging of Dangerous Substances Annex VI to Regulation (EC) No 1272/2008 [Online] http://esis.jrc.ec.europa.eu/ (accessed on May 10, **2011**).

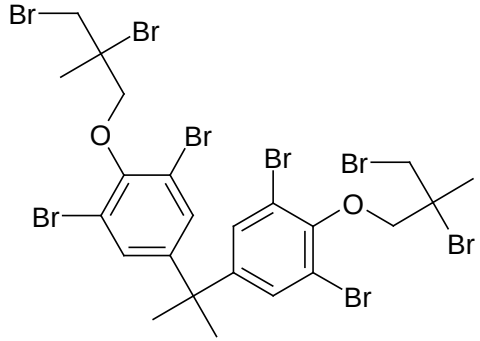
TBBPA-bis brominated ether derivative

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH)* were assigned using values from predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

§ Based on analogy to experimental data for a structurally similar compound. ¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.
¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
TBBPA-bis brominated ether derivative¥	97416-84-7	***L***§	***M***§	***M***§	***M***§	***M***§	***L***	***M***§	***L***§		***L***	***L***	***L***	***L***	***H***	***H***

TBBPA-bis brominated ether derivative



CASRN: 97416-84-7

MW: 971.68

MF: $C_{23}H_{24}Br_8O_2$

Physical Forms:
Neat: Solid

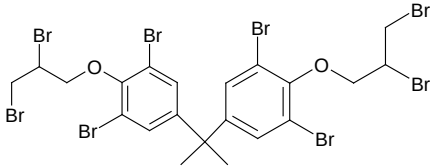
Use: Flame retardant

SMILES: BrCC(Br)(C)COc1c(Br)cc(C(C)(C)c2cc(Br)c(OCC(Br)(C)CBr)c(Br)c2)cc1Br

Synonyms: Benzene, 1,1'-(1-methylethylidene)bis[3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)] (CA Index Name for CASRN 97416-84-7); 1,1'-(Isopropylidene)bis(3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)benzene); 1,1'-Propane-2,2-diylbis[3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)benzene]; 1,3-Dibromo-5-[2-[3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)phenyl]propan-2-yl]-2-(2,3-dibromo-2-methylpropoxy)benzene; 2,2-Bis[4-(2,3-dibromopropoxy)-3,5-dibromophenyl] propane.

Trade Names: PYROGUARD SR-130; SR-130

Chemical Considerations: This is a discrete organic chemical with a MW <1,000. EPI v 4.0 was used to estimate physical/chemical and environmental fate values as required. No measured values were incorporated into the estimations.

Polymeric: No **Oligomers:** Not applicable	
Metabolites, Degradates and Transformation Products: None identified; although this compound contains a TBBPA backbone, degradation of this compound to TBBPA has not been demonstrated in a published study. The hazards of the theoretical degradation products were not considered in this hazard assessment.	
Analog: TBBPA bis(2,3-dibromopropyl) ether (CASRN 21850-44-2) **Endpoint(s) using analog values:** Acute Mammalian Toxicity, Genotoxicity, Repeated Dose Effects **Analog:** Confidential analog **Endpoint(s) using analog values:** Acute Mammalian Toxicity, Carcinogenicity, Reproductive and Developmental Toxicity, Repeated Dose Effects, Skin Sensitization	**Analog Structure:**  Tetrabromobisphenol A bis(2,3-dibromopropyl) ether (CASRN 21850-44-2)
Structural Alerts: Polyhalogenated aromatic hydrocarbons, Immunotoxicity (EPA, 2011a)	
Risk Phrases: Not classified by Annex VI Regulation (EC) No. 1272/2008 (ESIS, 2011)	
Hazard and Risk Assessments: None identified	

TBBPA-bis brominated ether derivative CASRN 97416-84-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	Approximately 115 (Measured)	Eurosarm MSDS, 2010	Reported for PYROGUARD SR-130, containing approximately 100% CASRN 97416-84-7.
	Approximately 110 (Measured)	DKS, 2012	Reported for the commercial product PYROGUARD SR-130 (≥90.4% purity of TBBPA-bis brominated ether derivative CASRN 97416-84-7); no study details provided.
Boiling Point (°C)	>300 (Estimated by analogy)	EPI; EPA, 1999	Decomposition is expected before the boiling point is reached based on analogy to TBBPA bis(2,3-dibromopropyl) ether. This value is the cutoff for high boiling point compounds according to HPV assessment guidance.
	260 decomposes (Measured)	DKS, 2012	Reported for the commercial product PYROGUARD SR-130 (≥90.4% purity of TBBPA-bis brominated ether derivative CASRN 97416-84-7); no study details provided.
Vapor Pressure (mm Hg)	$<3.3 \times 10^{-6}$ at 25°C (Measured)	ICL-IP, 2011	No experimental details were provided; however, this value is consistent with expected values based on the chemical structure and is adequate as an upper limit.
Water Solubility (mg/L)	$<4.2 \times 10^{-4}$ at 25°C (Measured)	ICL-IP, 2011	No experimental details were provided; however, this value is consistent with expected values based on the chemical structure and is adequate as an upper limit.

TBBPA-bis brominated ether derivative CASRN 97416-84-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	$<1x10^3$ (Measured)	Eurosarm MSDS, 2010	Nonspecific value reported as < 1 g/L for PYROGUARD SR-130, containing approximately 100% CASRN 97416-84-7.
	0.020 (Measured)	DKS, 2012	Reported for the commercial product PYROGUARD SR-130 (≥90.4% purity of TBBPA-bis brominated ether derivative CASRN 97416-84-7); no study details provided.
Log K_{ow}	12 (Estimated)	EPI; EPA, 1999	Estimated value is greater than the cutoff value, >10, according to methodology based on HPV assessment guidance.
Flammability (Flash Point)	Non-flammable (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis	DfE assessment methodology indicates that chemicals that contain both halogens and aromatic rings have the potential to form potentially hazardous compounds under high temperature conditions (Estimated)	Professional judgment	Based on analysis of the chemical structure.
pH	Not applicable	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
pK_a	Not applicable	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
HUMAN HEALTH EFFECTS				
Toxicokinetics		**The toxicokinetic properties of TBBPA-bis brominated ether derivative are estimated based on experimental data for the analog TBBPA bis(2,3-dibromopropyl) ether, for a closely related confidential compound, and by professional judgment. TBBPA-bis brominated ether derivative is expected to have similar toxicological properties based on structural similarities to the analogs. As a neat material, TBBPA-bis brominated ether derivative is estimated to not be absorbed through the skin and to have poor skin absorption when in solution; it is estimated to have poor absorption via the lungs and gastrointestinal tract. An experimental study in rats showed that the majority (95%) of the analog, TBBPA bis(2,3-dibromopropyl) ether, was rapidly eliminated in the feces following single or multiple oral doses with gastrointestinal absorption slow and minimal. However, when absorption did occur through the gastrointestinal tract, the analog TBBPA bis(2,3-dibromopropyl) ether was slowly eliminated from the blood, with the liver being the main organ for deposition.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as a neat material and poor absorption through skin when in solution; poor absorption through the lung and gastrointestinal tract; expected to be a poor alkylating agent due to low water solubility (Estimated by analogy)	Professional judgment	Based on a closely related confidential analog with similar structure and functional groups.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Following single or repeated (5 or 10 days) oral administration of 20 mg/kg [^{14}C]-TBBPA bis(2,3-dibromopropyl) ether to male F-344 rats, the compound was poorly absorbed from the gastrointestinal tract and uptake to the systemic circulation was considered slow. The C_{max} (0.6 µg/mL) occurred 7.4 hours after dosing. Distribution to the tissues accounted for <1% of the dose at 96 hours, while 95% of the dose (in [^{14}C] equivalents) was excreted in the feces within 36 hours of administration. Elimination in the urine accounted for <0.1% of the administered dose, and 1% of the dose (as metabolites) was excreted in the bile after 24 hours. (Estimated by analogy)	Knudsen et al., 2007; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether; study details reported in primary source.
Acute Mammalian Toxicity		**LOW: Estimated based on analogy to TBBPA bis(2,3-dibromopropyl) ether. Available experimental oral and dermal LD_{50} values for the analog TBBPA bis(2,3-dibromopropyl) ether are >2,000 mg/kg and an inhalation LC_{50} value for the analog is >20 mg/L.**		
Acute Lethality	**Oral**	Mouse LD_{50} >20,000 mg/kg (Estimated by analogy)	IPCS, 1995; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether; limited study details reported in a secondary source.
	Dermal	Mouse LD_{50} >20,000 mg/kg (Estimated by analogy)	IPCS, 1995; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether; limited study details reported in a secondary source.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Inhalation	Mouse LC_{50} >87,000 mg/m^3 (87 mg/L) (Estimated by analogy)	Great Lakes Chemical Corporation, 1982b; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether; limited study details reported in a secondary source.
Carcinogenicity		**MODERATE: No data located. Estimated to have potential for carcinogenicity based on the potential for alkylation and professional judgment.**		
	OncoLogic Results			No data located.
	Carcinogenicity (Rat and Mouse)	Potential for carcinogenic effects based on the potential for alkylation, although this compound is expected to be a poor alkylating agent due to low water solubility (Estimated by analogy)	Professional judgment	Based on a closely related confidential analog with similar structure and functional groups; expected to be a poor alkylating agent; however, there is still potential for alkylating activity.
	Combined Chronic Toxicity/ Carcinogenicity			No data located.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Genotoxicity		**MODERATE: Estimated based on analogy to TBBPA bis(2,3-dibromopropyl) ether. The analog TBBPA bis(2,3-dibromopropyl) ether was mutagenic to *Salmonella typhimurium* but did not cause chromosomal aberrations in Chinese hamster ovary (CHO) cells (*in vitro*), was negative in an *in vivo* micronucleus assay in mice and did not produce unscheduled DNA synthesis in rats.**		
	Gene Mutation *in vitro*	Positive, Ames assay (standard plate) in *Salmonella typhimurium* strains TA1535 and TA100 with and without metabolic activation and TA98 without metabolic activation (Estimated by analogy)	Great Lakes Chemical Corporation, 1982a; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether.
	Gene Mutation *in vivo*			No data located.
	Chromosomal Aberrations *in vitro*	Negative chromosomal aberrations in Chinese hamster ovary (CHO) cytogenetic assay with and without metabolic activation (precipitation was observed at the highest concentration) (Estimated by analogy)	IPCS, 1995; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether.
	Chromosomal Aberrations *in vivo*	Negative for micronucleated polychromatic erythrocytes in B6C3F1 mice (Estimated by analogy)	NTP, 2011; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether.
	DNA Damage and Repair	Negative for unscheduled DNA synthesis assay in Sprague-Dawley rats at 10, 50, 100, 500 and 1,000 µg/mL (Estimated by analogy)	IPCS, 1995; Professional judgment	Estimated based on data for the analog TBBPA bis(2,3-dibromopropyl) ether.
	Other (Mitotic Gene Conversion)			No data located.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Reproductive Effects		**MODERATE: Estimated based on a mechanistic consideration of its potential to act as an alkylating agent using professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	Although this compound is likely to be a poor alkylating agent due to low water solubility, the potential exists for alkylation. Based on mechanistic considerations of this potential for alkylation, there is potential for reproductive effects. (Estimated by analogy)	Professional judgment	Based on a closely related confidential analog with similar structure and functional groups; expected to be a poor alkylating agent; however, there is still potential for alkylating activity.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.
Developmental Effects		**MODERATE: Estimated based on a mechanistic consideration of its potential to act as an alkylating agent using professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	Although this compound is likely to be a poor alkylating agent due to low water solubility, the potential exists for alkylation. Based on mechanistic considerations of this potential for alkylation, there is potential for developmental effects. (Estimated by analogy)	Professional judgment	Based on closely related confidential analogs with similar structures and functional groups; expected to be a poor alkylating agent, however, there is still potential for alkylating activity.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Neurotoxicity		**LOW: Low potential for neurotoxicity estimated based on expert judgment. No data located.**		
	Neurotoxicity Screening Battery (Adult)	Low potential for neurotoxicity (Estimated)	Expert judgment	Estimated based on expert judgment.
Repeated Dose Effects		**MODERATE: Estimated based on analogy to a confidential analog. There is also potential for liver toxicity as TBBPA-bis brominated ether derivative is a highly brominated compound.**		
		Potential for liver effects based on a mechanistic consideration of this highly brominated compound (Estimated by analogy)	Professional judgment	Based on a closely related confidential analog with similar structure and functional groups.
		Mice were administered TBBPA bis(2,3-dibromopropyl) ether in their diet at 200 or 2,000 mg/kg-day for 90 days. There were no deaths or gross abnormalities (Estimated by analogy)	IPCS, 1995; Professional judgment	Based on the analog TBBPA bis(2,3-dibromopropyl) ether; limited study details reported in a secondary source.
Skin Sensitization		**LOW: No data located. Estimated to have low potential for skin sensitization based a closely related confidential analog and professional judgment. There is some potential for skin sensitization based on a mechanistic consideration of the potential for alkylation.**		
	Skin Sensitization	Potential for skin sensitization based on a mechanistic consideration of the potential for alkylation, although this compound is expected to be a poor alkylating agent due to low water solubility (Estimated by analogy)	Professional judgment	Based on a closely related confidential analog with similar structure and functional groups; expected to be a poor alkylating agent; however, there is still potential for alkylating activity.
		Not sensitizing, guinea pigs (Estimated by analogy)	Submitted Confidential Study	Estimated by analogy to a closely related confidential analog. Reported in a submitted confidential study; Study conducted according to GLP.
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Estimated not to cause eye irritation based on expert judgment. No experimental data located.**		

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Eye Irritation	Low potential for eye irritation (Estimated)	Expert judgment	Estimated based on expert judgment.
Dermal Irritation		**LOW: Estimated not to cause dermal irritation based on expert judgment. No experimental located.**		
	Dermal Irritation	Low potential for dermal irritation (Estimated)	Expert judgment	Estimated based on expert judgment.
Endocrine Activity		**Estimated based on analogy to TBBPA bis(2,3-dibromopropyl) ether. Based on four *in vitro* assays, the analog TBBPA bis(2,3-dibromopropyl) ether can interact with the endocrine system. The analog TBBPA bis(2,3-dibromopropyl) ether may have potential estrogenic and transthyretin-binding effects; it appears to inhibit sulfation of estradiol (E2), but does not exhibit estrogenic activity via interference with estrogen receptors (ER); it does not appear to interfere with aryl hydrocarbon receptor (AhR)-mediated, androgenic or progestagenic pathways. The analog TBBPA bis(2,3-dibromopropyl) ether competed with thyroid hormone precursor thyroxine (T4) for binding to human transthyretin (TTR), but did not exhibit thyroid hormone (T3) mimicking activity.**		
		Negative; did not cause inhibition of CYP17 catalytic activity in human H295R adrenocortical carcinoma cells (Estimated by analogy)	Cantón et al., 2006; Professional judgment	Based on the analog TBBPA bis(2,3-dibromopropyl) ether; data taken from primary study.
		Positive for estradiol sulfotransferase (E2SULT)-enzyme inhibition in E2SULT assay (Estimated by analogy)	Hamers et al., 2006; Professional judgment	Based on the analog TBBPA bis(2,3-dibromopropyl) ether; data taken from primary study.
		Negative for agonistic and antagonistic interactions with AhR, androgen, progesterone and estrogen receptors in series of CALUX assays (Estimated by analogy)	Hamers et al., 2006; Professional judgment	Based on the analog TBBPA bis(2,3-dibromopropyl) ether; data taken from primary study.
		Positive for displacement of thyroid hormone precursor T4 from plasma transport protein in TTR binding assay (Estimated by analogy)	Hamers et al., 2006; Professional judgment	Based on the analog TBBPA bis(2,3-dibromopropyl) ether; data taken from primary study.
		Negative for potentiating and antagonistic activity with T3-mediated cell proliferation in T-screen (Estimated by analogy)	Hamers et al., 2006; Professional judgment	Based on the analog TBBPA bis(2,3-dibromopropyl) ether; data taken from primary study.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Potential for immunotoxicity based on the presence of the polyhalogenated aromatic hydrocarbons structural alert and professional judgment.**		
	Immune System Effects	Potential for immunotoxicity based on the presence of the polyhalogenated aromatic hydrocarbons structural alert	EPA, 2011a; Professional judgment	Estimated based on the presence of a structural alert.
ECOTOXICITY				
ECOSAR Class		Halo Ethers		
Acute Aquatic Toxicity		**LOW: Based on estimated acute toxicity values for fish, Daphnid, and green algae that suggest no effects at saturation (NES).**		
Fish LC_{50}		Fish 96-hour LC_{50} = 3.01×10^{-6} mg/L ECOSAR class: Halo ethers	ECOSAR v. 1.10	NES: The log K_{ow} of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints.
		Fish 96-hour LC_{50} = 3.47×10^{-7} mg/L ECOSAR class: Neutral organics	ECOSAR v. 1.10	NES: The log K_{ow} of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0.; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

TBBPA-bis brominated ether derivative CASRN 97416-84-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Daphnid LC_{50}	Daphnid 48-hour LC_{50} = 1.33×10^{-6} mg/L ECOSAR class: Neutral organics	ECOSAR v. 1.10	NES: The log K_{ow} of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae EC_{50}	Green Algae 96-hour = 1.31×10^{-6} mg/L ECOSAR class: Neutral organics	ECOSAR v. 1.10	NES: The log K_{ow} of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Chronic Aquatic Toxicity	**LOW: Based on estimated chronic toxicity values for fish, Daphnid, and green algae that suggest NES.**		
Fish ChV	Fish ChV = 1.68×10^{-7} mg/L ECOSAR class: Halo ethers	ECOSAR v. 1.10	NES: The log of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints.

TBBPA-bis brominated ether derivative CASRN 97416-84-7			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish ChV = 1.06×10^{-7} mg/L ECOSAR class: Neutral organics	ECOSAR v. 1.10	NES: The log K_{ow} of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV	Daphnid ChV = 7.33×10^{-7} mg/L ECOSAR class: Neutral organics	ECOSAR v. 1.10	NES: The log K_{ow} of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Green Algae ChV	Green Algae ChV = 4.59×10^{-5} mg/L ECOSAR class: Neutral organics	ECOSAR v. 1.10	NES: The log K_{ow} of 12.4 for this chemical exceeds the SAR limitation for the log K_{ow} of 8.0; NES are predicted for these endpoints. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE			

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Transport		**TBBPA-bis brominated ether derivative is expected to have low mobility in soil based on estimations indicating strong absorption to soil. If released to the atmosphere, TBBPA-bis brominated ether derivative is likely to exist solely as particulate. Therefore, atmospheric removal will occur through wet or dry deposition as opposed to atmospheric oxidation. Based on the Henry's Law constant, volatilization from water or moist soil is not expected to occur at an appreciable rate. Fugacity models indicate that TBBPA-bis brominated ether derivative will partition predominantly to soil.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	EPI; Professional judgment	Cutoff value for non-volatile compounds.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; EPA, 2005	Cutoff value for non-mobile compounds.
	Level III Fugacity Model	Air = <1% (Estimated) Water = 5% Soil = 95% Sediment = <1%	EPI	These results were obtained without incorporating measured values; suitable experimental values were not available.
Persistence		**HIGH: High persistence of TBBPA-bis brominated ether derivative is expected. Aerobic biodegradation is not expected to be an important removal process, based on analog data. Although anaerobic biodegradation (by dehalogenation) may occur, the rate is likely to be low, and any such transformation will only lead to intermediate products that have essentially the same environmental properties. In other words, if emission to the environment occurs at any rate greater than negligible, this substance will accumulate. TBBPA-bis brominated ether derivative will exist primarily in the particulate phase in the atmosphere and is not expected to undergo removal by gas-phase oxidation reactions; however due to its properties, it is not expected to be released or transported to the atmosphere to a significant degree. TBBPA-bis brominated ether derivative is not anticipated to undergo removal by hydrolysis, since it does not contain hydrolyzable functional groups.**		
Water	**Aerobic Biodegradation**	Recalcitrant (Primary survey model) Recalcitrant (Ultimate survey model)	EPI	Not expected to be an important fate process.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	Based on the magnitude of the estimated Henry's Law constant.
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	Based on the magnitude of the estimated Henry's Law constant.
Soil	**Aerobic Biodegradation**			No data located.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Anaerobic Biodegradation	Probable (Anaerobic-methanogenic biodegradation probability model)	EPI	Not expected to be an important fate process.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	8.3 hours (Estimated)	EPI	Estimate for gas-phase process. Given that the material is expected to exist as a particulate in the atmosphere, the rate of this process will be attenuated, and it is not expected to be an important fate process.
Reactivity	**Photolysis**			No data located.
	Hydrolysis	Not a significant fate process (Estimated)	Mill, 2000; Professional judgment	The substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
Environmental Half-life		>180 days (Estimated)	PBT Profiler; EPI	Half-life estimated for the predominant compartment (soil), as determined by EPI and the PBT Profiler methodology.

TBBPA-bis brominated ether derivative CASRN 97416-84-7				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Bioaccumulation		**HIGH: High potential for bioaccumulation based on an estimated BAF of 1,600.**		
	Fish BCF	<76-94 at a concentration of 0.001 mg/L; <9-45 at a concentration of 0.01 mg/L in Carp *(Cyprinus carpio)* According to "Bioconcentration test of chemical substances in fish and shellfish" (Japanese notification, Yakushokuhatsu 0331 No.7, Heisei 23.03.29 Seikyoku No.5, Kanpokihatsu No.110331009, March 31, 2011; latest revision, April 2, 2012) and OECD Test Guideline 305C (Measured)	DKS, 2012	This test is most appropriately applied to organic chemicals with K_{ow} values of 1.5-6.0; the experimental set up did not include exposure through food. Reported for the commercial product PYROGUARD SR-130 (≥90.4% purity of TBBPA-bis brominated ether derivative CASRN 97416-84-7).
	BAF	1,600 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		No data located.		
Ecological Biomonitoring		No data located.		
Human Biomonitoring		This chemical was not included in the NHANES biomonitoring report (CDC, 2011).		

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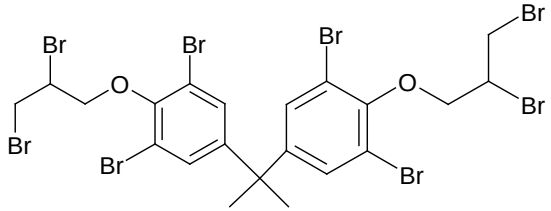
TBBPA bis(2,3-dibromopropyl) ether

VL = Very Low hazard L = Low hazard M = Moderate hazard H = High hazard VH = Very High hazard — Endpoints in colored text (VL, L, M, H, and VH) were assigned based on empirical data. Endpoints in black italics *(VL, L, M, H,* and *VH)* were assigned using values from predictive models and/or professional judgment.
This table contains hazard information for each chemical; evaluation of risk considers both hazard and exposure. Variations in end-of-life processes or degradation and combustion by-products are discussed in the report but not addressed directly in the hazard profiles. The caveats listed below must be taken into account when interpreting the information in the table.

¥ Aquatic toxicity: EPA/DfE criteria are based in large part upon water column exposures which may not be adequate for poorly soluble substances such as many flame retardants that may partition to sediment and particulates.

Chemical	CASRN	Human Health Effects											Aquatic Toxicity		Environmental Fate	
		Acute Toxicity	Carcinogenicity	Genotoxicity	Reproductive	Developmental	Neurological	Repeated Dose	Skin Sensitization	Respiratory Sensitization	Eye Irritation	Dermal Irritation	Acute	Chronic	Persistence	Bioaccumulation
TBBPA bis(2,3-dibromopropyl) ether¥	21850-44-2	L	*M*	M	*M*	*M*	*L*	*M*	L		L	L	L	*L*	VH	*H*

TBBPA bis(2,3-dibromopropyl) ether



CASRN: 21850-44-2

MW: 943.62

MF: $C_{21}H_{20}Br_8O_2$

Physical Forms:
Neat: Solid

Use: Flame retardant

SMILES: O(c1c(cc(cc1Br)C(c1cc(c(OCC(Br)CBr)c(c1)Br)Br)(C)C)Br)CC(Br)CBr

Synonyms: Benzene, 1,1'-(1-methylethylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)-; 1,1'-(1-Methylethylidene)bis(3,5-dibromo-4-(2,3-dibromopropoxy))benzene; 1,1'-(1-Methylethylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)]benzene; 1,1'-(Isopropylidene)bis(3,5-dibromo-4-(2,3-dibromopropoxy)benzene); 1,1'-(isopropylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)benzene]; 1,1'-propane-2,2-diylbis[3,5-dibromo-4-(2,3-dibromopropoxy)benzene]; 2,2-Bis[3,5-dibromo-4(2,3-dibromopropoxy)phenyl]propane; 2,2-Bis[3,5-dibromo-4-(2,3-dibromopropyloxy)phenyl]propane; 2,2-Bis[4-(2,3-dibromopropoxy)-3,5-dibromophenyl]propane; 3,3’,5,5’-TetrabromobisphenolA bis92,3-dibromopropyl) ether; 4,4’-Isopropylidenebis[2,6-dibromo-1-(2,3-dibromopropoxy)benzene]; 403AF; Bis(2,3-dibromopropoxy)tetrabromobisphenol A; Bromcal 66.8; Bromkal 66-8; D 5532; Dibromopropydian; FG 3100; FR 720; Fire guard 3100; Flame Cut 121K; Flame Cut 121R; GX 5532; Propane, 2,2-bis[3,5-dibromo-4-(2,3-dibromopropoxy)phenyl]-; PE-68; Pyroguard SR 720; SR 720; SAYTEX HP-800 A; HP-800 AG; HP-800 AGC; Tetrabromobisphenol A bis(2,3-dibromopropyl ether); Tetrabromobisphenol A bis(2,3-dibromopropyl) ether; Tetrabromobisphenol-A-bis-2,3-dibromopropyl ether Tetrabromobisphenol-A-bis-2,3-dibromopropylether; TBBPA-DBPE

Chemical Considerations: This is a discrete organic chemical with a MW below 1,000. EPI v 4.0 was used to estimate physical/chemical and environmental fate values as required. Measured values for available endpoints were incorporated into the estimations.

Polymeric: No
Oligomers: Not applicable

Metabolites, Degradates and Transformation Products: None identified; although this compound contains a TBBPA backbone, degradation of this compound to TBBPA has not been demonstrated in a published study. The hazards of the theoretical degradation products were not considered in this hazard assessment.

Analog: No analog
Endpoint(s) using analog values: Not applicable

Analog Structure: Not applicable

Structural Alerts: Polyhalogenated aromatic hydrocarbons, immunotoxicity (EPA, 2011).

Risk Phrases: Not classified by Annex I Directive 67/548/European Economic Community & IUCLID (Pakalin et al., 2007).

Hazard and Risk Assessments: Risk assessment complete for TBBPA bis(2,3-dibromopropyl) ether by the European Chemicals Bureau in 2007 (Pakalin et al., 2007).

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
PHYSICAL/CHEMICAL PROPERTIES			
Melting Point (°C)	117 (Measured)	Tokyo Chemical Industry Co., 2010; ChemSpider, 2011	Selected value for assessment.
	114 (Measured)	NICNAS, 2001	Sufficient details were not available to assess the quality of this study; value reported in a secondary source.
	90-100 (Measured)	IPCS, 1995; Great Lakes Chemical Corporation, 1982a	These reported values may be for a commercial mixture.
	95 (Measured)	Mack, 2004	
	107.3 (Measured) Reported as a range 104.3-116.6 using Optical melting determination	ECHA, 2013	Nonguideline, non-good laboratory practice (GLP) study reported in a secondary source.
	113.39 (Measured) Differential scanning calorimeter	ECHA, 2013	Nonguideline, non-GLP study reported in a secondary source.
Boiling Point (°C)	Decomposition at >270 (Measured)	IPCS, 1995	Decomposition is expected before the boiling point is reached.
Vapor Pressure (mm Hg)	$2.2 \pm 0.15 \times 10^{-4}$ at 20°C Static test according to Organisation of Economic Cooperation and Development (OECD) TG 104 (Vapor pressure curve) and EU Method A.4 (Vapor Pressure); GLP study; Purity of test substance 95.1% (Measured)	ECHA, 2013	Guideline study reported for FR-720 in a secondary source.
	$<10^{-8}$ (Estimated)	EPI; EPA, 1999	Cutoff value for nonvolatile compounds according to HPV assessment guidance.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
Water Solubility (mg/L)	$<10^{-3}$ (Estimated)	EPI; EPA, 1999	Cutoff value for non-soluble compounds according to HPV assessment guidance.
	1×10^{3} (Measured)	IPCS, 1995	Inadequate; these values are not consistent with a nonpolar, highly brominated material with a MW near 1,000.
	$<1\times10^{3}$ (Measured)	NICNAS, 2001	
	<0.1 mg/L (Measured) Reported as 0.144 µg/L at 20°C using OECD TG 105 (Water solubility) column elution method; GLP-study; Radiochemical purity of test substance (^{14}C-TBBPA-DBPE) > 99%.	ECHA, 2013	Cutoff value from a guideline study reported in a secondary source.
Log K_{ow}	12 (Estimated)	EPI; EPA, 1999	Estimated value is greater than the cutoff value, >10, according to methodology based on HPV assessment guidance.
Flammability (Flash Point)	Autoignition: 740°C (Measured) Ignition produced orange flame; according to IEC 61241-2-1 Method B Minimum ignition; GLP study	ECHA, 2013	Nonguideline study; purity of test substance TDBPE 720 not stated. Reported in a secondary source.
	Autoignition: >500 mJ (Measured) No ignition was observed; according to IEC 61241-2-3 Minimum ignition energy; GLP study	ECHA, 2013	Nonguideline; purity of test substance TDBPE 720 not stated. Reported in a secondary source.
Explosivity	Not expected to form explosive mixtures with air (Estimated)	Professional judgment	No experimental data located; based on its use as a flame retardant.
Pyrolysis			No data located.
pH	Not applicable	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
pK_a		Not applicable	Professional judgment	Does not contain functional groups that are expected to ionize under environmental conditions.
HUMAN HEALTH EFFECTS				
Toxicokinetics		**TBBPA bis(2,3-dibromopropyl) ether, as a neat material, is estimated not to be absorbed through the skin, to have poor skin absorption when in solution, and to have poor absorption via the lungs and gastrointestinal tract. An experimental study in rats showed that the majority (95%) of TBBPA bis(2,3-dibromopropyl) ether is rapidly eliminated in the feces following single or multiple oral doses and absorption is slow and minimal. However, if absorbed, TBBPA bis(2,3-dibromopropyl) ether is slowly eliminated from the blood, with the liver being the main organ for deposition.**		
Dermal Absorption *in vitro*				No data located.
Absorption, Distribution, Metabolism & Excretion	**Oral, Dermal or Inhaled**	Not absorbed through the skin as a neat material and poor absorption through skin when in solution; poor absorption through the lung and gastrointestinal tract. (Estimated by analogy)	Professional judgment	Based on closely related confidential analogs with similar structures, functional groups, and physical/chemical properties.
		Following single or repeated (5 or 10 days) oral administrations of 20 mg/kg [^{14}C]-TBBPA bis(2,3-dibromopropyl) ether to male F-344 rats, the compound was poorly absorbed from the gastrointestinal tract and uptake to the systemic circulation was considered slow. The C_{max} (0.6 µg/mL) occurred at 7.4 hours after dosing. Distribution to the tissues accounted for <1% of the dose at 96 hours while 95% of the dose (in [^{14}C] equivalents) was excreted in the feces within 36 hours of administration. Elimination in the urine accounted for <0.1% of the administered dose and 1% of the dose (as metabolites) was excreted in the bile after 24 hours.	Knudsen et al., 2007; ECHA, 2013	Study details reported in primary source.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Other	Male Fischer-344 rats were dosed with TBBPA-DBPE by IV administration. Fecal excretion of [^{14}C] equivalents was 27% by 36h, 71% by 96h. Urinary elimination was minimal (<0.1%). A single peak that co-eluted with the standard of TBBPA-DBPE was detected in extracts of whole blood following IV administration. TBBPA-DBPE elimination from the blood was slow. Kinetic constants following IV dosing were: $t_{1/2b}$: 24.8h; CL_b: 0.1mL/min. Systemic bioavailability was 2.2%. Liver was the major site of disposition.	ECHA, 2013	Well conducted study. Not performed according to GLP and standard testing guidelines.
Acute Mammalian Toxicity		**LOW: Based on oral and dermal LD_{50} values >2, 000 mg/kg and an inhalation LC_{50} value >20 mg/L.**		
Acute Lethality	**Oral**	Mouse LD_{50} >20,000 mg/kg	IPCS, 1995	Limited study details reported in a secondary source.
		Rat oral LD_{50} > 2,000 mg/kg	ECHA, 2013	Sufficient study details reported in a secondary source. GLP study conducted using OECD guidelines.
	Dermal	Mouse LD_{50} >20,000 mg/kg	IPCS, 1995	Limited study details reported in a secondary source.
		Rat dermal LD_{50} > 2,000 mg/kg	ECHA, 2013	Sufficient study details reported in a secondary source. GLP study conducted using OECD guidelines.
	Inhalation	Mouse LC_{50} >87,000 mg/m^3 (87 mg/L)	Great Lakes Chemical Corporation, 1982b	Limited study details reported in a secondary source.
		Rat 1 hr-inhalation LC_{50} >24.4 mg/L; Whole-body exposure to dust.	ECHA, 2013	Sufficient study details reported in a secondary source.
Carcinogenicity		**MODERATE: No data located. Estimated to have potential for carcinogenicity based on the potential for alkylation and professional judgment.**		
	OncoLogic Results			No data located.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Carcinogenicity (Rat and Mouse)	There is potential for carcinogenicity effects based on a mechanistic consideration of the potential for alkylation (Estimated)	Professional judgment	Based on mechanistic considerations.
	Combined Chronic Toxicity/ Carcinogenicity			No data located.
Genotoxicity		**MODERATE: TBBPA bis(2,3-dibromopropyl) ether was mutagenic to *Salmonella typhimurium* in one assay, while it was negative in other assays in *S. Typhimurium and E. coli.* This substance was also negative for mutagenicity in mouse lymphoma cells. TBBPA bis(2,3-dibromopropyl) ether is also estimated to have potential for genotoxicity based on the potential for alkylation. TBBPA bis(2,3-dibromopropyl) ether did not cause chromosomal aberrations or sister chromatid exchanges in Chinese hamster ovary (CHO) cells (*in vitro*), was negative in an *in vivo* micronucleus assay in mice and did not produce unscheduled DNA synthesis in rats.**		
	Gene Mutation *in vitro*	There is potential for mutagenicity based on a mechanistic consideration of the potential for alkylation. (Estimated)	Professional judgment	Based on closely related confidential analogs with similar structures and functional groups.
		Positive, Ames assay (standard plate) in *Salmonella typhimurium* strains TA1535 and TA100 with and without metabolic activation and TA98 without metabolic activation.	Great Lakes Chemical Corporation, 1982a; ECHA, 2013	Sufficient study details reported.
		Negative, *Salmonella typhimurium* strains TA1535, TA1537, TA100 and TA98 and *Escherichia coli* Wp2*uvr*A with and without metabolic activation.	Submitted confidential study; ECHA, 2013	Reported in a submitted confidential study; Study conducted according to GLP
		Negative, mouse lymphoma L5178Y cells with and without metabolic activation.	Submitted confidential study; ECHA, 2013	Reported in a submitted confidential study; Study conducted according to GLP
	Gene Mutation *in vivo*			No data located.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
	Chromosomal Aberrations *in vitro*	Negative chromosomal aberrations in Chinese hamster ovary (CHO) cytogenetic assay with and without metabolic activation (precipitation was observed at the highest concentration).	IPCS, 1995	Reported in a secondary source.
		Negative, sister chromatid exchanges in Chinese hamster ovary (CHO) cells with and without metabolic activation.	Submitted confidential study	Reported in a submitted confidential study; Study conducted according to GLP
	Chromosomal Aberrations *in vivo*	Negative for micronucleated polychromatic erythrocytes in B6C3F1 mice.	NTP, 2011; ECHA, 2013	Reported in a secondary source.
	DNA Damage and Repair	Negative for unscheduled DNA synthesis assay in Sprague Dawley rats at 10, 50, 100, 500 or 1,000 µg/mL.	IPCS, 1995	Reported in a secondary source.
	Other (Mitotic Gene Conversion)	Negative, unscheduled DNA synthesis, rat hepatocytes.	Submitted confidential study	Reported in a submitted confidential study; Study conducted according to GLP
Reproductive Effects		**MODERATE: Estimated to have potential for reproductive effects based on the potential for alkylation and professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	There is potential for reproductive effects based on a mechanistic consideration of the potential for alkylation (Estimated)	Professional judgment	Based on mechanistic considerations.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Reproduction and Fertility Effects			No data located.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Developmental Effects		**MODERATE: Estimated to have potential for developmental effects based on the potential for alkylation and professional judgment.**		
	Reproduction/ Developmental Toxicity Screen	There is potential for developmental effects based on a mechanistic consideration of the potential for alkylation (Estimated)	Professional judgment	Based on mechanistic considerations.
	Combined Repeated Dose with Reproduction/ Developmental Toxicity Screen			No data located.
	Prenatal Development			No data located.
	Postnatal Development			No data located.
Neurotoxicity		**LOW: Estimated not to have potential for neurotoxicity based on expert judgment; no data located.**		
	Neurotoxicity Screening Battery (Adult)	Low potential for neurotoxicity. (Estimated)	Expert judgment	Estimated based on expert judgment.
Repeated Dose Effects		**MODERATE: There is potential for liver toxicity because TBBPA bis(2,3-dibromopropyl) ether is a highly brominated compound and potential for immunotoxicity associated with polyhalogenated aromatic hydrocarbon structure. Located data were insufficient.**		
		Potential for liver effects based on a mechanistic consideration of this highly brominated compound (Estimated)	Professional judgment	Based on closely related confidential analogs with similar structures and functional groups.
		Mice were administered TBBPA bis(2,3-dibromopropyl) ether in their diet at 200 or 2,000 mg/kg-day for 90 days. No deaths, or abnormal symptoms observed in gross pathological examination. NOAEL = 2,000 mg/kg-day (highest dose tested)	IPCS, 1995; ECHA, 2013	Limited study details reported in a secondary source. Reported study details were not sufficient to evaluate the study quality and were considered insufficient to determine a hazard designation.
		Potential for immunotoxicity based on polyhalogenated aromatic hydrocarbons structure.	EPA, 2011; Professional judgment	Estimated based on the presence of a structural alert.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Skin Sensitization		**LOW: Not a skin sensitizer in guinea pigs. There is potential for skin sensitization based on the potential for alkylation.**		
	Skin Sensitization	There is potential for skin sensitization based on a mechanistic consideration of the potential for alkylation.	Professional judgment	Based on mechanistic considerations.
		Not sensitizing, guinea pigs	Submitted confidential study; ECHA, 2013	Reported in a submitted confidential study; Study conducted according to GLP
Respiratory Sensitization		**No data located.**		
	Respiratory Sensitization			No data located.
Eye Irritation		**LOW: Minimal eye irritation in rabbits clearing within 48 hours.**		
	Eye Irritation	Low potential for eye irritation. (Estimated)	Expert judgment	Estimated based on expert judgment.
		Workers report development of eye irritation following exposure to a complex mixture of airborne contaminants that included TBBPA bis(2,3-dibromopropyl) ether.	Great Lakes Chemical Corporation, 1999	Evidence is based on isolated incidents and workers were exposed to a complex mixture of airborne contaminants while melt processing that uses thermoplastic resin formulators containing this substance as an additive.
		Minimal irritation, rabbits; irritation was reversed within 24-48 hours.	Submitted confidential study; ECHA, 2013	Reported in a submitted confidential study; Study conducted according to GLP and OECD guidelines.
Dermal Irritation		**LOW: Not a skin irritant in rabbits.**		
	Dermal Irritation	Low potential for dermal irritation. (Estimated)	Expert judgment	Estimated based on expert judgment.
		Negative, rabbits	Submitted confidential study; ECHA, 2013	Reported in a submitted confidential study; Study conducted according to GLP and OECD guidelines.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Workers report development of dermal irritation following exposure to a complex mixture of airborne contaminants that included TBBPA bis(2,3-dibromopropyl) ether.	Great Lakes Chemical Corporation, 1999	Evidence is based on isolated incidents and workers were exposed to a complex mixture of airborne contaminants while melt processing that uses thermoplastic resin formulators containing this substance as an additive.
Endocrine Activity	**Based on 4 *in vitro* assays, TBBPA bis(2,3-dibromopropyl) ether can interact with the endocrine system. TBBPA bis(2,3-dibromopropyl) ether may have potential estrogenic and transthyretin-binding effects. TBBPA bis(2,3-dibromopropyl) ether appears to inhibit sulfation of estradiol (E2), but does not exhibit estrogenic activity via interference with estrogen receptors (ER). TBBPA bis(2,3-dibromopropyl) ether also does not appear to interfere with AhR-mediated, androgenic or progestagenic pathways. TBBPA bis(2,3-dibromopropyl) ether competed with thyroid hormone precursor thyroxine (T4) for binding to human transthyretin (TTR), but did not exhibit thyroid hormone (T3) mimicking activity.**		
	Negative; did not cause inhibition of CYP17 catalytic activity in human H295R adrenocortical carcinoma cells.	Cantón et al., 2006	Data taken from primary study.
	Positive for estradiol sulfotransferase (E2SULT)-enzyme inhibition in E2SULT assay.	Hamers et al., 2006	Data taken from primary study.
	Negative for agonistic and antagonistic interactions with aryl hydrocarbon (AhR), androgen (AR), progesterone (PR), and estrogen (ER) receptors in series of CALUX assays.	Hamers et al., 2006	Data taken from primary study.
	Positive for displacement of thyroid hormone precursor thyroxine (T4) from plasma transport protein in TTR binding assay.	Hamers et al., 2006	Data taken from primary study.
	Negative for potentiating and antagonistic activity with T3-mediated cell proliferation in T-screen.	Hamers et al., 2006	Data taken from primary study.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Immunotoxicity		**Potential for immunotoxicity based on the presence of polyhalogenated aromatic hydrocarbon structure and professional judgment.**		
	Immune System Effects	Potential for immunotoxicity based on the presence of polyhalogenated aromatic hydrocarbon structure. (Estimated)	EPA, 2011; Professional judgment	Estimated based on the presence of a structural alert.
ECOTOXICITY				
ECOSAR Class		Halo ethers		
Acute Aquatic Toxicity		**LOW: Based on experimental and estimated acute toxicity values for fish, daphnid, and algae that suggest no effects at saturation (NES).**		
Fish LC_{50}		Fish 96-hour LC_{50} = 1.5×10^{-5} mg/L (Estimated) ECOSAR: Halo ethers	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the structure activity relationship (SAR) limitation for log K_{ow} of 5.0; NES are predicted.
		Fish 96-hour LC_{50} = 2.2×10^{-6} mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
		Fish (*Oryzias latipes*) 96-hour LC_{50} > 500 mg/L; Semi-static conditions.	ECHA, 2013	Sufficient study details reported in a secondary source. GLP study conducted using OECD and Japanese guidelines. The value exceeds the estimated water solubility; NES are predicted.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Fish (*Oncorhynchus mykiss*) 96-hour LC_{50} > 100 mg/L; Static conditions.	ECHA, 2013	Sufficient study details reported in a secondary source. GLP study conducted using OECD guidelines. The value exceeds the estimated water solubility; NES are predicted.
Daphnid LC_{50}	Daphnia 48-hour LC_{50} = 3.01×10^{-6} mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 5.0; NES are predicted. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
	Daphnia magna 48-hour EC_{50} > 100 mg/L; Water accommodated fraction (WAF) nominal concentration.	ECHA, 2013	Sufficient study details reported in a secondary source. GLP study conducted using OECD guidelines. The value exceeds the estimated water solubility; NES are predicted.
Green Algae EC_{50}	Green algae 96-hour EC_{50} = 8.48×10^{-5} mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 6.4; NES are predicted. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2			
PROPERTY/ENDPOINT	**DATA**	**REFERENCE**	**DATA QUALITY**
	Green algae (*Pseudokirchneriella subcapitata*) 48 and 72-hour EC_{50} (growth rate/biomass) > 100 mg/L; WAF nominal concentration.	ECHA, 2013	Sufficient study details reported in a secondary source. GLP study conducted using OECD guidelines. The value exceeds the estimated water solubility; NES are predicted.
Chronic Aquatic Toxicity	**LOW: Based on estimated chronic toxicity values for fish, daphnid and green algae that suggest NES.**		
Fish ChV	Fish ChV = 8.78×10^{-7} mg/L (Estimated) ECOSAR: Halo ethers	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted.
	Fish ChV = 6.6×10^{-7} mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
Daphnid ChV			
	Daphnid ChV = 3.38×10^{-6} mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Green Algae ChV		Green Algae ChV = 0.00016 mg/L (Estimated) ECOSAR: Neutral organics	ECOSAR version 1.11	NES: The log K_{ow} of 12 for this chemical exceeds the SAR limitation for log K_{ow} of 8.0; NES are predicted. Narcosis classes (neutral organics) are provided for comparative purposes; DfE assessment methodology will use the lowest estimated toxicity value provided by ECOSAR classes that have a more specific mode of action relative to narcosis.
ENVIRONMENTAL FATE				
Transport		**Evaluation of TBBPA bis(2,3-dibromopropyl) ether transport is based entirely on estimations from quantitative structure activity relationships. TBBPA bis(2,3-dibromopropyl) ether is expected to have low mobility in soil based on estimations indicating strong absorption to soil. If released to the atmosphere, TBBPA bis(2,3-dibromopropyl) ether is likely to exist solely as particulate. As a particulate, atmospheric oxidation is not expected to be a significant route of environmental removal. Based on the Henry's Law Constant, volatilization from water or moist soil is not expected to occur at an appreciable rate. Level III fugacity models indicate that TBBPA bis(2,3-dibromopropyl) ether will partition predominantly to sediment and soil.**		
	Henry's Law Constant (atm-m^3/mole)	$<10^{-8}$ (Estimated)	EPI; Professional judgment	Cutoff value for nonvolatile compounds.
	Sediment/Soil Adsorption/Desorption Coefficient – K_{oc}	>30,000 (Estimated)	EPI; EPA, 2005	Cutoff value for nonmobile compounds.
		>30,000 (Measured) Reported as log K_{OC} >>5.63at 25°C; OECD TG 121: Estimation of Adsorption Coefficient on Soil and Sewage Sludge (HPLC); GLP-study	ECHA, 2013	Guideline study reported in a secondary source, although the experimental values were outside the scope of the protocol (log K_{OC} 1.5-5.0); radiochemical purity of test substance (TBBPA-bis(2,3-dibromopropyl ether)) >99%.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		>30,000 (Measured) Reported as log K_{OC} values of 6.1 (soil) and 7.6 (sludge) at pH 7.0; OECD Guideline 121: Estimation of Adsorption Coefficient on Soil and Sewage Sludge (HPLC); GLP-study	ECHA, 2013	Guideline study reported in a secondary source, although the experimental values were outside the scope of the protocol (log K_{OC} 1.5-5.0); purity of test substance (FR-720) not stated.
	Level III Fugacity Model	Air: <1% (Estimated) Water = 5% Soil = 95% Sediment: <1%	EPI	
Persistence		**VERY HIGH: High persistence of TBBPA bis(2,3-dibromopropyl) ether is expected as a result of located biodegradation studies and the absence of other expected likely removal processes under environmental conditions. In the course of a 28-day Japanese Ministry of International Trade and Industry (MITI) test, only 1% of TBBPA bis(2,3-dibromopropyl) ether was degraded. TBBPA bis(2,3-dibromopropyl) ether will exist primarily in the particulate phase in the atmosphere and is not expected to undergo removal by gas phase oxidation reactions. It is also not anticipated to undergo removal by hydrolysis.**		
Water	**Aerobic Biodegradation**	1% after 4 weeks OECD 301C; test concentration of 100 mg/L and concentration of activated sludge inoculum of 30 mg/L (Measured)	MITI, 2007	Adequate, guideline study.
		Passes Ready Test: No Test method: OECD TG 301B: CO_2 Evolution Test 1% degradation after 29 days using an activated sludge inoculum. (Measured)	ECHA, 2013	Adequate, guideline study reported in a secondary source; purity of test substance FR-720 is 95%.
	Volatilization Half-life for Model River	>1 year (Estimated)	EPI	
	Volatilization Half-life for Model Lake	>1 year (Estimated)	EPI	

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
Soil	**Aerobic Biodegradation**	0% degradation after 120 days in soil; OECD TG 307:Aerobic and Anaerobic Transformation in Soil; test concentration of 70.0 kBq/40 g soil dry weight; GLP-study (Measured)	ECHA, 2013	Adequate guideline study reported in a secondary source with ^{14}C-TBBPA-DBPE. No transformation products were observed; degradation assessed with 4 different soil types.
	Anaerobic Biodegradation	0% degradation after 100 days in natural sediment; OECD TG 308: Aerobic and Anaerobic Transformation in Aquatic Sediment Systems; GLP-study (Measured)	ECHA, 2013	Adequate, guideline study reported in a secondary source with ^{14}C-TBBPA-DBPE.Degradation results assessed with 2 sediment types, material mass balance was reported for both types: 1.98% in water and 84.48% in sediment.
	Soil Biodegradation w/ Product Identification			No data located.
	Sediment/Water Biodegradation			No data located.
Air	**Atmospheric Half-life**	12 hours (Estimated)	EPI	
Reactivity	**Photolysis**			No data located.
	Hydrolysis	50%/>1 year at 50°C and pH 4, 7, and 9 OECD TG 111: Hydrolysis as a function of pH and OPPTS 835.21 10: Hydrolysis as a function of pH; GLP study		Adequate, guideline study reported in a secondary source. Test substance purity (PE-68; CASRN 21850-44-2) not stated, no degradation was observed after 5 days in triplicate samples prepared for each pH level. The substance does not contain functional groups that would be expected to hydrolyze readily under environmental conditions.
Environmental Half-life		>180 days (Estimated)	PBT Profiler; EPI	Half-life estimated for the predominant compartment (soil), as determined by EPI and the PBT Profiler methodology.

TBBPA bis(2,3-dibromopropyl) ether CASRN 21850-44-2				
PROPERTY/ENDPOINT		**DATA**	**REFERENCE**	**DATA QUALITY**
		Aquatic mesocosm study; a controlled source of TBBPA bis(2,3-dibromopropyl) ether was applied and analyzed by GC-MS over the course of the study. TBBPA bis(2,3-dibromopropyl) ether was detected in both the particulate and sediment compartments. Degradation products were detected but not all were identified. (Measured)	de Jourdan, et al., 2013	Nonguideline field study providing supporting data about the partitioning and fate/persistence of this compound under environmental conditions.
Bioaccumulation		**HIGH: Based on an estimated BAF of 12,000 and its detection in Great Lakes Herring gull eggs, potential for bioaccumulation is high.**		
	Fish BCF	3.4 to 43 (15 µg/L concentration) <17 to 130 (1.5 µg/L concentration) (Measured)	MITI, 2007	Adequate, guideline study.
	BAF	12,000 (Estimated)	EPI	
	Metabolism in Fish			No data located.
ENVIRONMENTAL MONITORING AND BIOMONITORING				
Environmental Monitoring		TBBPA bis(2,3-dibromopropyl) ether was identified in dust collected near an artificial stream and pond system in Berlin, Germany (Harju et al., 2009); in sewage sludge samples from southern China; in sediments from southern China (Shi et al., 2009) and in water, sediment and soil along the Liuyang River in China (Qu et al., 2011).		
Ecological Biomonitoring		Detected in Great Lakes Herring gull eggs (Letcher and Chu, 2010).		
Human Biomonitoring		This chemical was not included in the National Health and Nutrition Examination Survey biomonitoring report (CDC, 2011).		

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5 Summary of Hazard Assessments, Considerations for Selecting Flame Retardants, and an Overview of Alternative Materials

This chapter outlines attributes that a decision-maker should consider in choosing an alternative to hexabromocyclododecane (HBCD), including hazard, social, performance, and economic considerations as they prepare to make substitution decisions. An overview of alternative insulation materials and the applications in which they may be used is also included.

5.1 Considerations for Selecting Flame Retardants

Design for the Environment (DfE) alternatives assessments provide extensive information on chemical hazards and discuss other general factors that are relevant to substitution decisions. When selecting flame retardants, decision-makers will consider performance and cost in combination with the human health and environmental information from this report.

This alternatives assessment considers three alternatives to HBCD. One of the alternatives, a butadiene styrene brominated copolymer, is a polymer with a molecular weight (MW) much greater than 10,000 daltons. The other two, a tetrabromobisphenol A (TBBPA)-bis brominated ether derivative and TBBPA bis(2,3-dibromopropyl) ether, are large molecules with a MWs close to 1,000 daltons. All three of these chemicals incorporate bromine as the mechanism for fire retardation and are the only known technically viable options for HBCD in polystyrene foam insulation. The limited number of alternatives is, at least in part, due to the requirement that flame retardants for expanded polystyrene (EPS) and extruded polystyrene (XPS) foam (1) allow the material to comply with fire safety codes, (2) not compromise the physical properties of the foam, and (3) be compatible with its manufacturing processes and formulas. The availability of flame retardants for polystyrene is described in Section 3.2.

5.1.1 Hazard Considerations

There are five general attributes evaluated in this assessment that can inform decision-making about the potential hazards associated with chemical alternatives: (1) human health hazard, (2) ecotoxicity, (3) persistence, (4) bioaccumulation potential, and (5) exposure potential. In general, a “safer” chemical alternative has lower potential for human health hazard, lower ecotoxicity, better degradability, low potential for bioaccumulation, and lower exposure potential compared to substances currently used. The hazard assessments are summarized below; readers are encouraged to review the individual detailed hazard profiles of each chemical in Chapter 4.

While experimental data were available for almost all hazard endpoints for HBCD (the exception is respiratory sensitization), experimental data for some or all of the hazard endpoints for the three alternatives were not available or were deemed inadequate. In these cases, hazard values were assigned using data for structural analogs, structure activity relationship (SAR) modeling, and professional judgment based upon physical-chemical properties and knowledge of data for similar chemicals. In some cases (e.g., respiratory sensitization), it was not possible to assign hazard values due to a lack of data, models, or structural analogs. It should be noted that those

hazard designations based on estimated effect levels are regarded with a lower level of confidence compared to hazard designations based on measured data. Empirical data would allow for a more robust assessment that would confirm or refute professional judgment and thus support a more informed choice of alternatives. Estimated values in the report can, therefore, also be used to prioritize data needs.

Human health hazard: The DfE alternatives assessment criteria (U.S. EPA 2011a) address a consistent and comprehensive list of human health hazard endpoints for which DfE has established thresholds indicating levels of concern. These endpoints include acute toxicity, carcinogenicity, genotoxicity, reproductive toxicity, developmental toxicity, neurotoxicity, repeated dose toxicity, skin sensitization, respiratory sensitization, eye irritation, and dermal irritation.

HBCD has a High hazard designation for developmental toxicity, a Moderate hazard designation for reproductive and repeated dose effects, and an estimated Moderate hazard designation for carcinogenicity and neurotoxicity; other health endpoints have Low or Very Low hazard designations. Comparatively, the butadiene styrene brominated copolymer has Low hazard designations (either measured or estimated) for all health endpoints arising from its high MW and limited potential for absorption (U.S. EPA 2012b). The substance is marketed as greater than 60,000 daltons with negligible low MW components. U.S. Environmental Protection Agency (EPA) has regulated this polymer with a Significant New Use Rule (SNUR) that was finalized in June 2013. Manufacture (or import) of the polymer requires notification to EPA except in these cases: (1) the MW of the polymer is in the range of 1,000 to 10,000 daltons, or (2) the MW of the polymer is ≥10,000 daltons and less than 5 percent of the particles are in the respirable range of 10 microns or less (U.S. EPA 2013). The TBBPA-bis brominated ether derivative and TBBPA bis(2,3-dibromopropyl) ether have a Moderate hazard designation for carcinogenicity, genotoxicity, reproductive toxicity, developmental toxicity, and repeated dose toxicity; Low hazard designations were designated for acute toxicity, neurotoxicity, skin sensitization, eye irritation, and dermal irritation. Due to a lack of data for the substance, the hazard designations for the TBBPA-bis brominated ether derivative were all estimated. Available data for the structurally similar substance, TBBPA bis(2,3-dibromopropyl) ether (CASRN 21850-44-2), and a closely related confidential compound were used for the estimations based on analogy. Recently, TBBPA has been evaluated in a 2-year carcinogenicity study at the National Toxicology Program (NTP) (National Toxicology Program (NTP) 2013b). An updated DfE hazard profile for TBBPA may be published in 2014 as part of the report on Flame Retardants in Printed Circuit Boards (U.S. EPA 2008). Although derived from TBBPA, there are not any carcinogenicity data for TBBPA-bis brominated ether derivative or its analog TBBPA bis(2,3-dibromopropyl) ether. There is also a lack of data to determine if TBBPA might be a degradation product of TBBPA-bis brominated ether derivative. TBBPA bis(2,3-dibromopropyl) ether has been nominated for consideration for a 2-year cancer bioassay at NTP (Haneke 2002; National Toxicology Program (NTP) 2013a). Respiratory sensitization was not characterized for HBCD or the alternatives because no data were located, no suitable estimation methods were available, or no structural alerts were identified.

Ecotoxicity: Ecotoxicity includes adverse effects observed in wildlife. Aquatic organisms have historically been the focus of environmental toxicity considerations by industry and government

during industrial chemical review. Surrogate species of fish, aquatic invertebrates, and algae are traditionally assessed to consider multiple levels of the aquatic food chain. HBCD is aquatically toxic. Aquatic toxicity for the three alternatives is low, driven by their lack of appreciable water solubility leading to no effects at saturation (NES). This analysis does not consider dietary exposure to substances since guideline tests are focused on exposure from the water column. For the butadiene styrene brominated copolymer, TBBPA-bis brominated ether derivative and TBBPA bis(2,3-dibromopropyl) ether, aquatic toxicity is estimated to be low (NES) based upon its physical-chemical properties (poor water solubility and estimated high octanol-water partition coefficient (K_{ow}). A number of publications identified the presence of HBCD in a variety of terrestrial and aquatic species. There were few terrestrial ecotoxicity studies; these studies were not associated with High hazard. Therefore, potential for impacts of HBCD on high trophic level and terrestrial wildlife is unclear. The butadiene styrene brominated copolymer is not expected to be bioavailable; impacts on wildlife from the TBBPA-bis brominated ether derivative or TBBPA bis(2,3-dibromopropyl) ether have not been studied.

Persistence: Persistence describes the tendency of a chemical to resist degradation and removal from environmental settings, such as air, water, soil, and sediment. Chemical flame retardants must be stable by design in order to maintain their flame retardant properties. HBCD and the TBBPA-bis brominated ether derivative have High persistence designations. The butadiene styrene brominated copolymer and TBBPA bis(2,3-dibromopropyl) ether have Very High persistence designations. Highly persistent chemicals may ultimately degrade in the right environmental conditions, but time to degradation is on the order of months to years and could be much longer. An ideal flame retardant would be stable in the material to which it is added and have low toxicity, but also be degradable at the end of the material's use (i.e., persistent in use but not after use). This quality has been difficult to achieve for flame retardants. Long-term degradation products, though beyond the scope of this assessment, are also important to consider as they might be more toxic, bioaccumulative or persistent (PBT) than the parent compound. The TBBPA-bis brominated ether derivative and TBBPA bis(2,3-dibromopropyl) ether have a tetrabromobisphenol A (TBBPA) backbone. TBBPA-bis brominated ether derivative and TBBPA bis(2,3-dibromopropyl) ether could theoretically release TBBPA, however, no experimental studies describing this degradation pathway were found. As mentioned on the previous page, an updated DfE hazard profile for TBBPA may be published in 2014. HBCD has been found to degrade to tetrabromocyclododecene, dibromocyclododecadiene, or 1,5,9-cyclododecatriene by aerobic and anaerobic processes (Davis, Gonsior et al. 2006).

Bioaccumulation Potential: The ability of a chemical to accumulate in living organisms is described by the bioconcentration, bioaccumulation, biomagnification, and/or trophic magnification factors. Each of these indices has a different definition and as such, a substance that bioaccumulates does not necessarily biomagnify. HBCD was assigned a Very High hazard designation for bioaccumulation based on standardized test results for bioconcentration factor (BCF). Based on structure activity relationships (SARs), the potential for a molecule to be absorbed by an organism tends to be lower when the molecule is larger than 1,000 daltons. This is reflected in the estimated Low hazard designation for bioaccumulation for the butadiene styrene brominated copolymer. The TBBPA-bis brominated ether derivative and TBBPA bis(2,3-dibromopropyl) ether have an estimated High bioaccumulation designation based on their lipophilic log K_{ow} and expected slow rate of metabolism.

Exposure Potential: For humans, chemical exposure may occur at different points throughout the chemical and product life cycle; by dermal contact, by inhalation, and/or by ingestion; and is affected by multiple physical-chemical factors. The DfE alternatives assessment assumes exposure scenarios to chemicals and their alternatives within a functional use class are roughly equivalent. The assessment also recognizes that, in some instances, chemical properties, manufacturing processes, chemical behavior in particular applications, or use patterns may affect exposure scenarios. Stakeholders should evaluate carefully whether and to what extent manufacturing changes, life-cycle considerations, and physical-chemical properties will result in different patterns of exposure. Large polymeric flame retardants and those that are reacted into a polymer backbone can decrease exposure potential.

Exposure potential can also be impacted by the persistence and bioaccumulation potential of chemicals and/or their degradation products. Chemicals with both higher persistence and higher bioaccumulation potential generally have a higher potential for exposure than chemicals that do not possess both of these attributes. As was described above, all four of the chemicals in this assessment were assigned High or Very High persistence potential and all were assigned High or Very High bioaccumulation potential except for the butadiene styrene brominated copolymer, which, based on its large size and insolubility, has Very High persistence but Low bioaccumulation potential. Since the butadiene styrene brominated copolymer and the TBBPA-bis brominated ether derivative are new to the market, environmental monitoring or biomonitoring information are not available to inform the exposure potential of these two alternatives. The higher exposure potential based on higher persistence and higher bioaccumulation for the TBBPA-bis brominated ether is supported by data for the analog TBBPA bis(2,3-dibromopropyl) ether (CASRN 21850-44-2), a chemical also evaluated in this report that has been detected in environmental media (Harju, Heimstad et al. 2009; Shi, Chen et al. 2009; Qu, Shi et al. 2011) and gull eggs (Letcher and Chu 2010). In general the exposure potential to the butadiene styrene brominated copolymer is expected to be lower than the other chemicals in this assessment because it is a large polymer and is unlikely to be released from the polystyrene, in addition to its low likelihood of bioaccumulation. However, long-term fate in the environment is not understood; degradation products could have greater exposure potential upon release of the substance to the environment.

5.1.2 Social Considerations

Social considerations may impact the choice of alternative chemicals. This section highlights occupational, consumer, and environmental justice considerations. Stakeholders may identify additional social considerations for application to their own decision-making processes.

Occupational Considerations: Workers might be exposed to relatively high concentrations of flame retardant chemicals from direct contact when conducting specific tasks related to manufacturing, processing, and application of chemicals. For example, tasks that involve heat and pressure where materials are aerosolized as they are mixed and reacted may result in direct contact with flame retardant chemicals. Many facilities have established risk management

practices, which are required to be clearly communicated to all employees. The National Institute for Occupational Safety and Health (NIOSH) has established a hierarchy of exposure control practices[18]. Starting with the most protective, the practices are: elimination, substitution, engineering controls, administrative controls, and personal protection. Switching to inherently low hazard chemicals can benefit workers by decreasing workplace risks through the best exposure control practices: elimination and substitution of hazardous chemicals with safer alternatives.

Consumer and Lifestage Considerations: Consumers are potentially exposed to flame retardant chemicals through multiple pathways described in Chapter 2. Exposure research provides evidence that people carry body burdens of flame retardants, including HBCD. Individuals may also experience disproportionate impacts during certain lifestages resulting from higher exposures, increased susceptibility in response to exposure, or both conditions (National Academy of Sciences 2008). For example, children may be more susceptible to environmental exposures than adults because:

- Their bodily systems are still developing and exposures may occur during critical windows of susceptibility;
- Their bodies may absorb and process chemicals differently due to characteristics such as greater permeability of the blood-brain barrier, slower excretion from the kidneys, and alterations in the activity of metabolic enzymes;
- They eat more, drink more, and breathe more in proportion to their body size;
- Their behavior can expose them more to chemicals and organisms, for example, hand-to-mouth and object-to-mouth behaviors (Xue, Zartarian et al. 2007); and
- They may be exposed to chemicals, including HBCD, in human milk (Landrigan, Sonawane et al. 2002; Covaci, Gerecke et al. 2006; Arnot, McCarty et al. 2009).

Prenatal development represents a potential window of susceptibility whereby exposures to chemicals in the environment can contribute to adverse pregnancy and developmental outcomes (Stillerman 2008). During prenatal development, biological systems are forming, and disruption of these processes can have consequences later in life. While the placenta is designed to protect the fetus from stressors, including chemical exposures, chemicals (including HBCD) have been shown to pass through this organ resulting in prenatal exposures (Myren, Mose et al. 2006; Meijer, Weiss et al. 2008).

Environmental Justice Considerations: At EPA, environmental justice concerns refer to disproportionate impacts on minority, low-income, or indigenous populations. These disproportionate impacts arise because these population groups may experience higher exposures, are more susceptible in response to exposure, or experience both conditions. Factors that are likely to influence resilience/ability to withstand harm from a toxic exposure can vary with sociodemographics (e.g., co-morbidities, diet, metabolic enzyme polymorphisms, etc.) and are therefore important considerations. Adverse outcomes associated with exposure to chemicals

[18] http://www.cdc.gov/niosh/topics/engcontrols/

may be disproportionately borne by minority and low income populations. Additional information about EPA's environmental justice policy can be accessed at: www.epa.gov/compliance/ej/resources/policy/considering-ej-in-rulemaking-guide-07-2010.pdf.

Some populations have higher exposures to certain chemicals in comparison to the average member of the general population. A recent study has found that Hispanics, non-Hispanic African Americans, and non-Hispanic Asians generally experience greater exposure to certain chemical components associated with adverse health outcomes than non-Hispanic whites (Bell and Ebisu 2012). The same study found that populations with lower socioeconomic statuses generally experienced higher estimated exposures to certain chemicals based on education, unemployment, poverty, and earnings (Bell and Ebisu 2012). Higher exposures to environmental chemicals may also be attributable to atypical product use patterns and exposure pathways. This may be due to a myriad of factors such as cultural practices, language and communication barriers, and economic conditions. The higher exposures may also be a result of:

- The proximity of these populations to sources that emit the environmental chemical (e.g., manufacturing industries, industries that use the chemical as production input, hazardous waste sites, etc.);
- Access to and use of consumer products that may result in additional exposures to the chemical; or
- Higher employment of these groups in occupations associated with exposure to the chemical.

Finally, certain populations may experience high exposures to toxic chemicals due to geography, food sources, and cultural practices. For example, research shows that Alaska Natives are disproportionately impacted by certain flame retardants and other persistent organic pollutants (POPs), both because of atmospheric transport of persistent chemicals and because of the biomagnification of chemicals in traditional subsistence food webs (Arctic Monitoring and Assessment Program 2009).

5.1.3 Performance and Cost Considerations

The DfE approach allows companies to examine hazard profiles of potential replacement chemicals so they can consider the human health and environmental attributes of a chemical in association with cost and performance considerations. This is intended to allow companies to develop marketable products that meet performance requirements while reducing risk associated with potential hazard and exposure attributes. While DfE does not assess performance considerations, these attributes are critical to the overall function and marketability of flame retardants.

As was discussed in Chapter 2, the performance requirements for EPS and XPS foam used as insulation are governed by the American Society for Testing and Materials (ASTM) C578,

Standard Specification for Rigid, Cellular Polystyrene Insulation.[19] In addition to meeting the required flammability standards, these requirements include density, R-value, compressive strength, flexural strength, water vapor transmission rate, water absorption, and dimensional stability. Alternatives must also be compatible with the manufacturing processes for EPS and XPS (e.g., the high pressures and temperatures of the XPS manufacturing process). Substituting chemicals can involve significant costs, as industries must adapt their production processes and have products re-tested for all required performance and product standards. Handling, disposal, and treatment costs may also be important considerations when evaluating alternatives. The expenses associated with initial alternative substitution may ultimately result in reduced costs associated with managing consumer concerns and public perceptions of hazardous chemicals.

Information on the cost and availability of butadiene styrene brominated copolymer is based on a 2012 report by the Persistent Organic Pollutants Review Committee (POPRC) (Persistent Organic Pollutants Review Committee 2012). According to the POPRC report, cost estimates for EPS and XPS containing this flame retardant versus HBCD have been made by various parties. One manufacturer does not anticipate EPS containing the butadiene styrene brominated copolymer to have a significant impact on its cost competitiveness with other products. However, other parties expect that the cost of using the butadiene styrene brominated copolymer instead of HBCD in EPS and XPS can lead to cost increases. One party suggests the costs of using the alternative are 90% (EPS) to 120% (XPS) higher than when using HBCD. The impact of the butadiene styrene brominated copolymer on the price of EPS and XPS will remain unclear until the alternative is fully commercialized. Regarding availability, the butadiene styrene brominated copolymer is currently commercially available through a single manufacturer but is expected to be available through two additional manufacturers in 2014. With this increased production capacity, it is anticipated that the butadiene styrene brominated copolymer suppliers will have sufficient capacity to replace HBCD in polystyrene foams in three to five years.

Consideration of economic factors is often better addressed by decision-makers within the context of their organization. Accurate cost estimations must be company-specific; the impact of substituting chemicals on complex product formulations can only be analyzed in-house and a company must determine for itself how changes will impact market share or other business factors.

5.2 Alternative Materials

This section is intended to provide a general overview of alternative insulation materials and their applications. The Partnership discussed alternative insulation materials and decided to include general information on this topic. This section is not a comprehensive comparison of alternative insulation materials. Some of these alternative materials may require flame retardants that are characterized in other DfE alternatives assessments. However, this section does not include a chemical hazard assessment of the alternatives. While this report provides general

[19] Likewise, ASTM D6817 applies to polystyrene foams in geotechnical engineering applications ("geofoam"). See www.astm.org/search/site-search.html?query=C578#84513999.

information about these potential alternatives, their inclusion here is informational only. Inclusion of a substance or material in a DfE report does not denote environmental preferability.

There are several insulation characteristics that should be considered when selecting alternative insulation materials. These include environmental considerations, material safety considerations, performance considerations, and economic considerations, as discussed below.

Environmental Considerations
Environmental considerations include whether the manufacturing process results in pollution, whether the material can be reused or recycled, and the environmental impacts of its end-of-life management. Another factor is the source of the insulation raw material: whether it is made from recycled or virgin materials and the environmental impacts associated with manufacturing the raw materials. It is important to consider the embodied energy of the product, such as the energy required to produce and transport materials (Wilson 1995), as well as the full range of environmental impacts (Wilson 1995; Wilson 2010a). All of these issues feed into the life-cycle considerations that should be taken into account when selecting insulation materials. Full life-cycle assessments (LCAs) are not within the scope of this report.

Material Safety Considerations
The material safety of the alternative insulation material is also a consideration. Insulation materials may use or contain hazardous chemicals, such as diisocyanates, or constituents such as blowing agents that may contribute to air pollution. Some materials pose health concerns as chemicals are released during processing, installation, or emitted throughout the life of the product. Whether the material contains PBT chemicals is also important, especially when the potential life-cycle impacts of the product are considered.

Performance Considerations
As discussed in Section 2.1.1, the primary desired properties of rigid foam and its alternatives include R-value, compressive strength, flexural strength dimensional stability, moisture resistance, and fire safety (e.g., flame spread index, smoke development index). In addition to these primary desired properties, other performance characteristics to consider when selecting alternatives include: water vapor transmission (permeance); corrosivity; weight of the material; resiliency; resistance to mold growth and microbial degradation; acoustical energy absorption; and whether the material can be used in retrofits and/or new construction. It is also important to note that for some materials, the R-value may decrease over the lifetime of the product (Minnesota Sustainable Housing Initiative 2007). Therefore, it is important to consider the expected lifespan of the product needed for the application.

Economic Considerations
Economic considerations, such as whether the material is readily available and its cost, will also impact the viability of alternative insulation materials. Return on investment, including payback through energy savings and net energy savings potential, are other economic considerations that may impact the decision to switch to alternative insulation materials.

The sections that follow provide information about specific insulation materials that could be used as substitutes for the functional uses of EPS and XPS. As was discussed in the previous

section, the functional use of EPS and XPS is for continuous insulation applications such as in walls and roofs on the exterior of buildings. These applications include products such as insulating concrete forms (ICFs); structural insulated panels (SIPs); below grade and geotechnical applications for foundations and highways; and other dimensional stability or strength applications, e.g., insulated cold storage applications.

5.2.1 Rigid Board Alternatives

This section discusses alternative insulation materials identified by stakeholders that are available as rigid board and therefore can be used in many of the same applications as EPS and XPS. EPS and XPS are types of board insulation, which is typically made from plastic foams or fibrous materials, and is available in the form of board sheets (Minnesota Sustainable Housing Initiative 2007; U.S. Department of Energy 2008). Other materials readily available as board insulation include polyisocyanurate foams, perlite insulation, and mineral wool/rockwool insulation. These materials are described below.

Non-flame retarded EPS or XPS is a potential alternative to flame retarded EPS or XPS if used in conjunction with a thermal (fire resistant) barrier. In this case, the flame retardancy would be provided by a fire resistant covering or coating that isolates the insulation materials within the building (Sall 2010). While coatings face several technical and economic hurdles, separate non-adhered coverings that have sufficient flame barrier properties can be used to render the flame retardant properties of the insulation unimportant. For example, in some countries, non-flame retarded EPS is used in ground or floor insulation below a concrete layer, or in wall cavities with thermal barriers (COWI 2011). EPS is readily available with no flame retardants to the food or packaging industry. U.S. manufacturers generally only supply building insulation that contain flame retarded resins so that fire safety and construction codes can be met, and to reduce fire hazards of EPS and XPS after manufacturing and during transportation and construction.

Polyisocyanurate foams are manufactured from petrochemical feedstocks and a blowing agent (e.g., pentane), and are most commonly available as sprayed foam or board insulation with a facer on each surface (Wilson 1995; Wilson 2005; U.S. Department of Energy 2011). Polyisocyanurate foams typically use 5-14% by weight tris(chlorpropyl) phosphate (TCPP) as a flame retardant to meet building codes (Wilson 2005). The performance requirements for faced polyisocyanurate foam board insulation are specified in ASTM C1289. Its thermal resistance, which is subject to thermal drift over time, is cited by the National Roofing Contractors Association as having an in-service R-value of 5.0 or 5.6 per inch depending on whether the board is exposed to heating or cooling conditions (Graham 2010). It is primarily used as roof insulation, but is also used in cavity walls and sheathing (Polyisocyanurate Insulation Manufacturers Association 2011). Polyisocyanurate foam board insulation used in walls can have an R-value as high as 6.5 per inch (The Dow Chemical Company 2013; The Dow Chemical Company n.d.). It should be noted that the isocyanates (e.g., methylene diphenyl diisocyanate (MDI), polymeric methylene diphenyl diisocyanate (pMDI) and toluene diisocyanate (TDI), or other isocyanate oligomers) used in the manufacture of the foam pose human health hazards and are the subject of an EPA Action Plan and a separate DfE Best Practices Partnership (U.S. EPA 2011b).

Perlite insulation is manufactured from naturally occurring volcanic minerals (Sustainable Sources 2011). It is available as a rigid board, but is also often used as loose fill insulation or concrete aggregate (Healthy Building Network 2011; Sustainable Sources 2011). Perlite insulation is naturally fire resistant and does not require a flame retardant (COWI 2011). The performance requirements for perlite insulation are specified in ASTM C728 which lists its R-value as 2.7 per inch. It is most often used in roofs and walls, but can be used in all building applications, including floors (COWI 2011; Healthy Building Network 2011; Sustainable Sources 2011).

Mineral wool/rockwool is available as a semi-rigid or rigid board, batt, and blown-in loose fill insulation (Wilson 2005; Sustainable Sources 2011). It is made from recycled steel slag and/or basalt rock, uses a phenol-formaldehyde binder (Wilson 2005; Sustainable Sources 2011), and contains trace amounts of formaldehyde (ICA Fittings 2011). Formaldehyde poses human health hazards. EPA is currently developing regulations to implement the Formaldehyde Standards for Composite Wood Products Act. Mineral wool does not require a flame retardant (Ehrlich 2009). It has a typical R-value of 4 (Ehrlich 2009). It can be used in cavity walls, roofing, exterior insulation, and below grade (Wilson 2005; Ehrlich 2009).

5.2.2 Alternatives for Certain Functional Uses

This section describes alternative insulation materials identified by stakeholders that may be used for certain functional uses of EPS and XPS. These alternatives are generally not available as rigid board insulation, but may be used in certain applications where the properties such as dimensional stability or compressive strength are not integral to the performance of the insulation material. Types of insulation that may fulfill this purpose include:

- **Blanket insulation**, which is available in batts or rolls and is usually made from glass or mineral fibers (U.S. Department of Energy 2008). Blanket insulation is used in unfinished walls, foundations, floors, and ceilings and is fitted between studs, joists, and beams, or is laid on open horizontal surfaces (U.S. Department of Energy 2011). Blanket insulation may be used in place of some applications of board insulation in walls, floors, ceilings, and foundations.
- **Foamed-in-place insulation**, which is sprayed into cavities, reduces air leaks, and is usually made from polyurethane (Minnesota Sustainable Housing Initiative 2007; Wilson 2010b). Foamed-in-place insulation may be used in place of board insulation in applications such as walls or roofs where they can be sprayed to fill and seal cavities.
- **Loose-fill insulation**, **blown insulation**, and **sprayed insulation,** which are generally composed of loose fibers or fiber pellets that are blown into wall cavities or above horizontal ceiling surfaces using pneumatic equipment (U.S. Department of Energy 2008). Applications of loose-fill insulation include wall cavities, attic floors, irregularly shaped areas, and fill in around obstructions (U.S. Department of Energy 2008). Similar to foamed-in-place insulation, loose-fill, blown, and sprayed insulation may be used in place of board insulation in applications such as walls or roofs.

Alternative insulation materials within the categories of insulation types described above that may be used for certain functional uses of EPS and XPS are summarized below.

Cellulose is used as a type of blown-in loose-fill insulation and is made from recycled newspaper (Wilson 1995; COWI 2011). Ammonium sulfate, boric acid, and borax are typically used as flame retardants in cellulose insulation to meet building codes (Wilson 2005). It has a typical R-value of 3.7 and is not water resistant (Minnesota Sustainable Housing Initiative 2007; COWI 2011). There are also health concerns as printer ink in the newsprint may outgas as formaldehyde, as well as from inhalation of paper dust during installation (Greenspec 2010). Cellulose insulation is most commonly used as a loose-fill insulation in attic and wall cavities (Wilson 1993).

Cementitious foam is used as a foamed-in-place insulation and is made from magnesium oxide derived from seawater and talc (Wilson 2005). Cementitious foam does not require a flame retardant (Healthy Building Network 2011). It is has a typical R-value of 3.9 (AirKrete Inc 2009). Cementitous foam is friable, limiting its application (Wilson 2005). Currently, cementitious foam is manufactured by a single producer, limiting its distribution to the east coast of the United States (Wilson 2005; Healthy Building Network 2011). It is used to insulate walls, roofs, and ceilings (AirKrete Inc 2009).

Cotton insulation is available as a batt, and is made either from cotton and polyester mill scraps or from post-consumer recycled clothing, most often recycled denim scrap (Wilson 2005). It uses borate or ammonium sulfate flame retardants (Wilson 2005). Cotton insulation may absorb water and has a typical R-value of 3.4 (Healthy Building Network 2011; U.S. Department of Energy 2011). It can be used in the typical applications of batt insulation such as in walls, foundations, floors, and ceilings (U.S. Department of Energy 2011).

Fiberglass is available as a batt, blown-in loose fill, or semi-rigid board insulation material (Minnesota Sustainable Housing Initiative 2007). It is made from silica sand and may contain recycled glass content (Wilson 2005). Fiberglass insulation traditionally uses phenol formaldehyde binders, although some manufacturers are switching to acrylic or bio-based resins (Wilson 2005; Ehrlich 2010). Formaldehyde poses human health hazards and EPA is currently developing regulations to implement the Formaldehyde Standards for Composite Wood Products Act. Fiberglass does not require a flame retardant, although there are some specialty fiberglass batt products with halogenated flame retardants in the paper backing (Healthy Building Network 2011). It has a typical R-value of 3.2 (Minnesota Sustainable Housing Initiative 2007). It is used in masonry walls, cavity walls, roofs, attics, ceilings, and flooring (COWI 2011; Healthy Building Network 2011).

Polyurethane is most commonly available as a foam-in-place insulation (known as Spray Polyurethane Foam (SPF)) and is made from mixing two ingredients conventionally known as "Side A" and "Side B". Side A is composed of isocyanates; Side B is a polyol blend that contains a refined petroleum (often some bio-based content) with a blowing agent (typically either water or chlorofluorocarbons (CFCs)/ hydrofluorocarbons (HFCs) (historically), more recently non-ozone depleting/low global warming potential substances) and other additives such as surfactants, amines, and flame retardants (Wilson 2005; U.S. Department of Energy 2011; U.S. EPA 2012a). Some polyurethane insulations may use some bio-based content, which is generally less than 15% of the total content (BioBased Insulation 2012). Polyurethane insulation

uses TCPP or resorcinol-bis-diphenyl phosphate (RDP) as a flame retardant to meet building codes (Wilson 2005). Polyurethane has an R-value ranging from 3.6 to 7.5 (COWI 2011; U.S. Department of Energy 2011). It can be used to insulate cavities, walls, or roofs ("Foam-in-Place Polyurethane Insulation" 2008). It should be noted that exposures to diisocyanates (e.g., MDI) and other ingredients in SPF that may be found in vapors, aerosols, dust, or on surfaces during and for a period after installation may cause adverse health effects such as asthma (U.S. EPA 2011c). The EPA has issued an Action Plan for MDI and related compounds and performed separate DfE Best Practices Partnership on this topic (U.S. EPA 2011b). EPA has also developed an informational website addressing concerns for SPF use: http://www.epa.gov/dfe/pubs/projects/spf/spray_polyurethane_foam.html.

5.2.3 Specialty and Emerging Alternative Materials

The insulation materials presented in this section may be functional alternatives to EPS and XPS, but are not considered to be currently viable for large scale building applications, and so are constrained to specialty applications or limited geographic areas. This information is intended to provide context in case changes in manufacturing processes or economies of scale allow these products to become viable in the future.

Specialty and emerging alternative insulation materials identified by stakeholders include:

- **Aerogel** is available as a rigid board, roll, or loose-fill; and is used to insulate underfloors, rainscreens, roofing, cathedral ceilings, and interior walls (Madonik 2011). It is made from silica gel, polyethylene terephthalate (PET), fiberglass, and magnesium hydroxide (COWI 2011). Aerogel is lightweight and has a very high R-value of 10, but is costly.
- **Carbon foam** is a type of rigid board foam made from calcined coke. It is manufactured in limited quantities and is used primarily as a specialty insulation in the aeronautic, marine, and energy industries (Madonik 2011).
- **Foamglas** is a rigid board insulation made from sand, limestone, and soda ash that is primarily used for high-temperature industrial applications where extreme heat resistance is required but can be used to as insulation in roofs, walls, and below-grade. There is only one Foamglas manufacturer in the U.S. and Foamglas is costly compared to other rigid board insulation products (Wilson 2010c).
- **Phenolic foam** is a type of rigid foam and foamed-in-place insulation that may be used in roofing, wall cavities, external walls, and floors (COWI 2011). Currently, only foamed-in place phenolic insulation is available in the U.S (U.S. Department of Energy 2011). Rigid phenolic foams are no longer produced in the U.S. after corrosive breakdown products caused construction issues in the early 1990s, although they may be imported from Europe and Asia (Smith, Carlson et al. 1993; Schroer, Hudack et al. 2012).
- **Reflective insulation** is a foil-faced insulation material that incorporates a radiant barrier (normally highly reflective aluminum) with a kraft paper, plastic film, polyethylene bubble, or cardboard backing (U.S. Department of Energy 2012). Reflective insulation is used to reduce radiant heat flow across an open space, most usefully for downward radiant heat flow, and is typically used between roof rafters,

floor joists, and wall studs (U.S. Department of Energy 2008). The rest of the insulations described here are designed to reduce thermal heat conduction through solid surfaces in any direction. For this reason, reflective insulation is not an alternative for EPS and XPS, but rather works best in complement with other forms of insulation.

- **Agrifiber insulation** is manufactured from agricultural waste (e.g., rice hulls, fungal mycelia, wheat or rice straw) and is available as board insulation (Healthy Building Network 2011; Wilson 2011). Agrifiber typically uses borate as a flame retardant (Sustainable Sources 2011). New agrifiber insulations under development using mycelium as a binder are reported to have obtained a Class 1 fire rating without use of added chemical flame retardants (Wilson 2011). Agrifiber insulation has an R-value ranging from 3.0 to 3.5 and is not water resistant; it is currently available only in limited SIPs applications (Healthy Building Network 2011; Madonik 2011).

Further information about the alternative materials discussed in this section can be found in materials provided by the U.S. Department of Energy[20], Environmental Building News[21], The Pharos Project[22], GreenSpec[23], manufacturer websites, and the respective trade association websites, as well as the references cited above.

[20] http://www.energysavers.gov/your_home/insulation_airsealing/index.cfm?mytopic=11510
[21] http://www.buildinggreen.com/news/index.cfm
[22] http://www.pharosproject.net/
[23] http://www.greenspec.co.uk/insulation-introduction.php

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