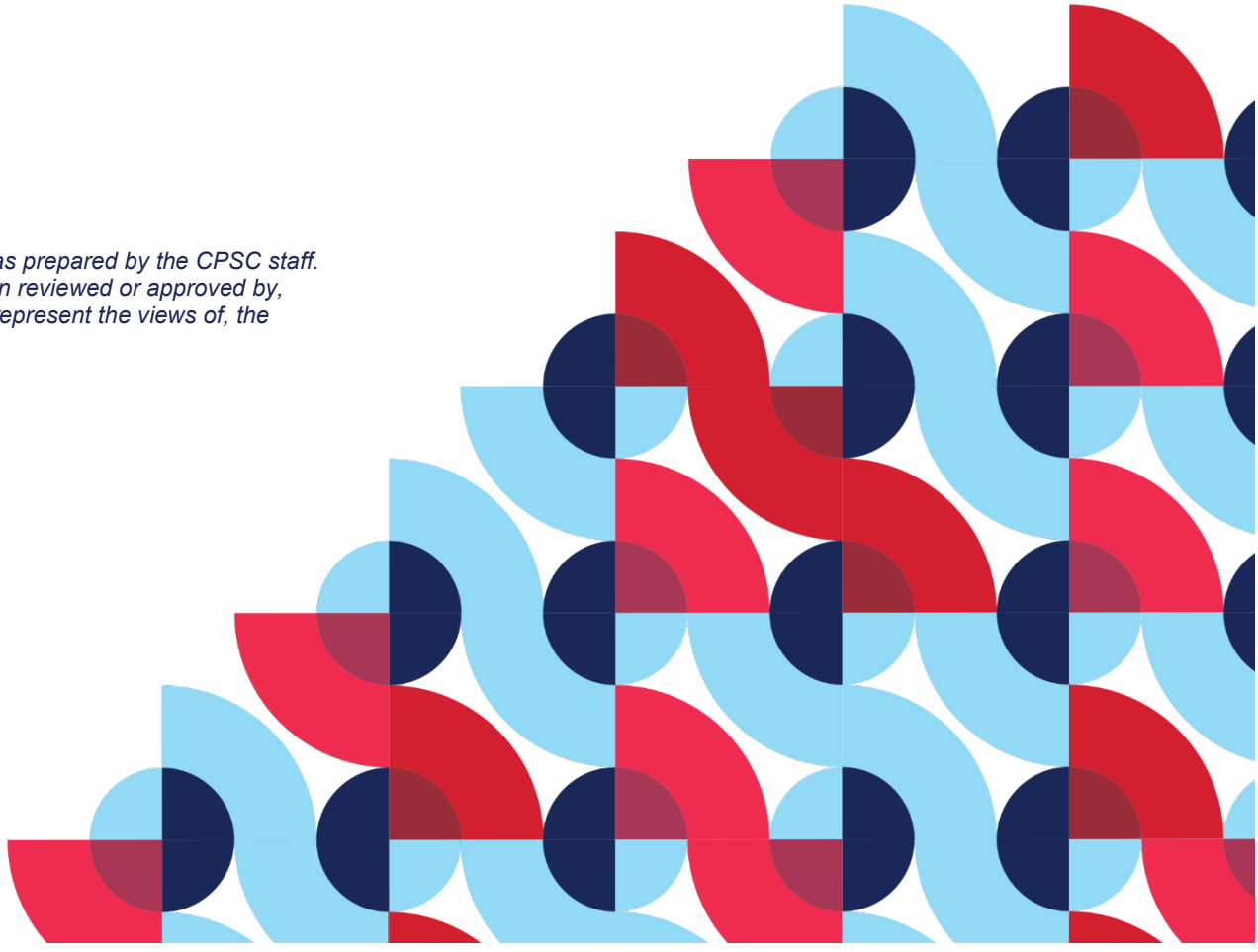
United States
Consumer Product Safety Commission

Organohalogen Flame Retardant Scope Document: Polyhalogenated Bisphenol Aliphatic and Functionalized Subclass

November 2023

This report was prepared by the CPSC staff. It has not been reviewed or approved by, and may not represent the views of, the Commission.



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1. Executive Summary

This scope document addresses the polyhalogenated bisphenol aliphatic and functionalized (PHBAF) subclass, one of 14 subclasses of organohalogen flame retardants (OFR). OFRs contain a carbon-halogen bond and are one of the main categories of flame retardants (FRs). FRs are substances that alter the normal degradation or combustion processes of materials. They are incorporated into materials or used on surfaces to reduce or eliminate the tendency to ignite when exposed to heat or flame for a short amount of time.

Informed by initial review of the market and use research, evidence maps, and availability of physicochemical data for the PHBAF subclass and its analogs, as well as the Criteria for Scoping Determination described in this document, Consumer Product Safety Commission (CPSC or Commission) staff concludes, at the time of writing, that the PHBAF subclass has sufficient data to proceed with risk assessment. Next steps, as resources are available, involve completing the hazard, dose-response, and exposure assessments before drafting the class-based risk assessment.

2. Introduction

This document contains the results of scoping efforts by CPSC staff to characterize readily available information on the chemistry, uses, human toxicity, exposure, and human health risk of members of the PHBAF subclass of OFRs. This document is one of the scope documents that CPSC staff is producing to address each of 14 OFR chemical subclasses.

The primary question answered by the scope documents is:

> *Can a risk assessment for this subclass be completed based on a combination of existing data and estimation (modeling) approaches?*

To answer this question, the scope document developed for each subclass outlines the criteria for determining sufficiency for hazard assessments and exposure assessments, describes the data available, and provides the scoping determination. If the answer to the question above is yes for that subclass, the scope document describes (i) CPSC staff's interpretation of available data through evidence maps and estimation approaches and (ii) the analysis plan and conceptual model that CPSC staff plans to follow to complete this assessment. These subclasses will then be prioritized for risk assessments.

If the answer is no, then the scope document for that particular subclass describes (i) CPSC staff's interpretation of available data through evidence maps and estimation approaches and (ii) key data gaps. These subclasses will be temporarily deprioritized for risk assessments.

For additional details on how the information contained in all scope documents was compiled, refer to the following CPSC companion documents:[1]

- Development of a Flame Retardant and an Organohalogen Flame Retardant Chemical Inventory
- Market and Use Report: Characterizing OFR Chemistries, Sources, and Uses in the U.S. and International Markets, Volumes 1 and 2 (Appendices)
- Literature Survey Guide: Approaches Taken to Develop Evidence Maps from Readily Available Databases, Completed Assessments, and Literature Reviews

3. Background

In 2015, several organizations and individuals petitioned CPSC (Petition HP 15-1) to ban the use of additive OFRs, as a class, in durable infant or toddler products, children's toys, childcare articles, or other children's products (other than car seats), residential upholstered furniture, mattresses and mattress pads, and the plastic casings of electronic devices. In 2017, the Commission voted to grant the petition to direct staff to convene a Chronic Hazard Advisory Panel,[2] and to complete a scoping and feasibility study in cooperation with the National Academy of Sciences, Engineering, and Medicine (NASEM).

NASEM established a committee of experts to address the charge and published the Committee's report, "A Class Approach to Hazard Assessment of Organohalogen Flame Retardants," in May 2019 (NASEM, 2019). The Committee first decided to determine whether the chemicals of interest can be defined as a single class or as subclasses, based on structure, physicochemical properties, biology, or a combination of characteristics. The Committee stated that if a class approach is viable, then the hazard assessment approach would be to survey the literature to determine availability of all types of toxicity data (human, animal, in vitro, other relevant studies) for all relevant toxicity end points. Then, if relevant data are available on any chemical of interest for a given end point, the plan would be to extract, evaluate, and integrate the data to reach a decision about potential hazards that can be applied to the entire class or subclass. The NASEM report stated that the Committee compared the OFR inventory to the analogues and found that the OFRs cannot be treated as a single class for the purposes of a CPSC hazard assessment. Rather, the Committee identified 14 subclasses of OFRs, based on chemical structure, physicochemical properties of the chemicals, and predicted biological activity.

[1] Project documents, including CPSC staff reports, contractor reports, and key references may be found on the CPSC Organohalogen Flame Retardant Chemicals Assessment website (https://www.cpsc.gov/Business--Manufacturing/Organohalogen-Flame-Retardant-Chemicals-Assessment) or Docket No. CPSC-2015-0022 (https://www.regulations.gov/docket/CPSC-2015-0022).
[2] CHAP review could occur prior to finalizing any subclass risk assessment if carcinogenicity, mutagenicity, reproductive/developmental toxicity or other chronic hazard were chosen as relevant endpoints.

In fiscal year 2020 (FY 2020), CPSC staff developed a process for assessing the risks of OFRs in consumer products. A staff report to the Commission (Staff Plan) (CPSC, 2020) builds on the recommendations from the NASEM committee and outlines options and recommendations for proceeding with the project in FY 2021 and beyond (subject to availability of resources). In brief, the Staff Plan outlined work that initially would establish procedures for class-based risk assessment of each OFR subclass, refine the chemicals and analogs for multiple OFR subclasses, identify data sources, and determine available toxicity, chemical use, and exposure information. Staff subsequently initiated several activities, largely through contractors and interagency collaborations, to begin work on the project.

4. Approach

4.1. Criteria for Scoping Determination

CPSC staff will determine whether a subclass has sufficient data to proceed, at this time, with risk assessment based on data availability. In this context, data availability among subclass members and among identified analog chemicals is characterized as "no data," "some data," or "data rich" for both hazard information and exposure information, with definitions of each category provided below.

4.1.1. Hazard

The criteria for sufficiency for hazard assessment for the subclass are:

- At least one data rich chemical among the subclass chemicals or analog chemicals, and
- Multiple chemicals with some data among subclass chemicals or analog chemicals with empirical short-term toxicity and other data (availability of modeled physicochemical and toxicity data can contribute to the determination).
- Only a minority of the substances in the subclass are "no data" substances.

The data availability categories are defined using the literature survey results as follows:

- Chemicals with no data:
    - No empirical data for physicochemical characteristics, and
    - No empirical data for toxicity, and
    - No or limited predicted/modeled physicochemical or toxicity data.
- Chemicals with some data (i.e., chemicals that are neither data rich nor have no data):
    - Some physicochemical data (may include empirical or modeled), and
    - No to limited traditional chronic/subchronic animal toxicity studies, and
    - Some short-term toxicity, in vitro, high-throughput, or other nonanimal data.

- Chemicals that are data rich:
    - Near complete empirical physicochemical data, and
    - Multiple traditional animal toxicity studies (i.e., acute, systemic repeated dose toxicity, or reproductive/developmental), and
    - Multiple short-term in vivo toxicity studies, and in vitro, high-throughput, or other nonanimal data, and
    - Available empirical data likely support derivation of a quantitative toxicity reference value(s).
    - Modeled toxicity data, if such data demonstrate close agreement with available empirical data, are acceptable to support this category, but such data are not required.
    - Availability of human data supports this category but is not required.

In addition to evaluating the amount and breadth of available data for each chemical in a subclass, CPSC staff plans to consider the availability of similar types of data for multiple subclass members (e.g., similar subchronic/chronic studies, similar endpoints evaluated, and similar short-term toxicity studies, in vitro assays, or mechanistic data). That is, CPSC staff plans to consider consistency in data availability across members of a subclass.

4.1.2. Exposure

The criteria for sufficiency for exposure assessment for the subclass are:

- At least one data rich chemical among the subclass chemicals for which average daily doses for human populations have been reported or can be estimated, and
- Multiple subclass chemicals with some data from environmental monitoring, biomonitoring, product testing, or any toxicokinetic studies (availability of modeled physicochemical, emissions, migration, occurrence, or disposition data can contribute to the determination).
- Note that subclass members classified as “no data” chemicals do not have sufficient information for exposure assessment.

The data availability categories are defined using the literature survey and market and use research results as follows:

- Chemicals with no data:
    - No market and use information indicating use as a flame retardant.
- Chemicals with some data (i.e., chemicals that are neither data rich nor have no data):
    - Some evidence (per market and use information) that it has been, currently is, or could be used as a flame retardant, and
    - Some physicochemical data (may include empirical or modeled), or
    - At least one experimental environmental monitoring, biomonitoring, product testing, or toxicokinetic study, or comparable modeling studies that provide information on estimated occurrence, emissions, or disposition, or
    - Existing or de novo modeled estimates of physicochemical properties, emissions, migration, occurrence, or disposition.

- Chemicals that are data rich:
    - Evidence (per market and use information) that it has been, currently is, or could be used as a flame retardant, and
    - Near complete empirical physicochemical data, and
    - Multiple environmental monitoring, biomonitoring, product testing, or toxicokinetic studies, and
    - Available empirical data support estimates of a quantitative average daily dose(s) for human exposure, and
    - Modeled exposure data (emissions, occurrence, disposition), if such data demonstrate close agreement with empirical data, are acceptable to support this category, but such data are not required.

4.2. Inventory

The NASEM committee, as part of its consideration of class approaches to hazard assessment, created an inventory of 161 OFRs and identified more than 1,000 analog chemicals (i.e., chemicals with similar functional, structural, and predicted biological activity) across 14 chemical subclasses. Subsequently, CPSC staff, in collaboration with the U.S. Environmental Protection Agency (EPA), refined a Quantitative-Structure-Use-Relationship (QSUR) model to predict the probability of whether a chemical is a flame retardant or an OFR. These efforts, in combination with market and use research, led to a manuscript, "Development of a Flame Retardant and an Organohalogen Flame Retardant Chemical Inventory," published in *Nature Scientific Data* (Bevington et al., 2022). This work identified additional OFR chemicals, resulting in an expanded inventory of 488 OFRs in 14 subclasses.

The OFR inventory completed by CPSC staff should not be considered a fixed and final list of all possible OFR chemicals. This project, including the market and use research and literature survey work, has used established identifiers for each chemical, such as CAS RN®,[3] DTXSID,[4] INCHIKEY,[5] PUBCHEM ID,[6] and SMILES,[7] as well as chemical names and common synonyms. However, even with identifiers that should uniquely describe chemicals, there are a few cases in the inventory of the same chemical identified in different ways. CPSC staff also acknowledges that some identifiers correspond to mixtures.[8] To the extent that information on chemicals would be located using different identifiers, CPSC staff will maintain separate listings; however, once

[3] CAS RN®, or CAS Registry Number®, is a unique identification number for individual chemical substances assigned by CAS, a division of the American Chemical Society.
[4] DTXSID, or DSSTox substance identifier, is an alphanumeric identifier for individual chemical substances used in the U.S. Environmental Protection Agency's CompTox Chemicals Dashboard.
[5] INCHIKEY, stands for International Chemical Identifier and is a unique 27-character identifier.
[6] PUBCHEM ID is a unique identifier specific to the National Library of Medicine's PUBCHEM database.
[7] Simplified molecular-input line-entry system (SMILES) describes the structure of a chemical in a way that can be used by a computer.
[8] See, for example, CAS RN 85535-84-8, which refers to a group of halogenated aliphatic chain chemicals with chain length from 10 to 13 carbons. Chemical names associated with this CAS RN include short chain chlorinated paraffins; alkanes, C10-13, chloro; and chlorinated paraffins, C10-13.

staff confirms that multiple records apply to a single chemical (or mixture), analyses of the chemical will consider the combined data for that chemical regardless of the identifiers.

CPSC staff also notes that the inventory may be modified through the course of the project as staff continues analyses of chemicals in each subclass and considers additional information. The result of additional analyses could be the removal or addition of chemicals to the inventory.

4.3. Market and Use Research

The OFR market and use research was intended to collect relevant information and data to (1) characterize each OFR subclass, (2) identify uses of chemicals in each OFR subclass, and (3) identify trends associated with each OFR subclass. CPSC staff sought information about production or consumption of OFR chemicals and identified uses in consumer products and other market information. CPSC staff also sought information on regulatory actions, including current and proposed laws, policies, and regulations related to OFR chemicals at international, federal, state, and local levels of government. Detailed descriptions of the approach and process are found in Volume 1 of the Market and Use Profile (see Appendix: Supporting Files) completed under a CPSC-sponsored contract. Briefly, the market and use research captured information from targeted scientific literature and gray literature, and from readily available data sources in other formats. Data sources included national chemical inventories, other government data, such as from required reporting of production and waste information for specified chemicals or other types of curated databases, and certain commercial sources.

4.3.1. Targeted Literature Search

Section 3.2.6 of the Market and Use Report explains the methodology used for the targeted literature search completed for the OFR market and use research. The targeted searches for literature related to the flame-retardant market identified sources of relevant material from databases, websites, or other online information repositories, and broader searches of internet-based sources using standard search tools such as Google Scholar and selected searches of commercial online literature databases (e.g., Dialog/ProQuest). Specifically, the contractor executed searches of 140 literature databases using the Dialog/ProQuest platform.[9]

Following a review of the source title and abstract, the contractor rated each identified source for relevance on a scale of 1 to 5, 5 being the most relevant, and obtained PDF copies of as many of the sources identified as possible, with priority given to those sources rated higher for relevance. Among all 255 sources obtained, the contractor prioritized the review of 187 complete sources.

For each PDF reviewed, the contractor highlighted information on topics of interest for the study, such as manufacturing or import activity, use of chemicals in products, lifecycle considerations, and regulatory or other trends. The report further identified all OFR chemicals discussed in the source, and where available, captured the CAS RN for each chemical and any synonyms, abbreviations, and trade names. From the 187 sources extracted and reviewed, the contractor

[9] For a list of data sources searched using Dialog/ProQuest, see Exhibit 3-32 of the Market and Use Report Volume 1.

made over 2,200 OFR identifications (for 488 unique OFRs). The summary of sources reviewed is provided in the Data Source Synthesis Excel workbook of the supplemental Market and Use Profile Supporting Files, referenced by OFR subclass.

4.3.2. Other Data Sources

The OFR Market and Use Report contains information collected from inventories and registries from the United States, Canada, Mexico, the EU, Japan, and China. In the United States, the Toxic Substances Control Act (TSCA) inventory was used to identify if an OFR substance was designated as active or inactive. In addition to determining whether OFR substances appear as active substances on the TSCA chemical inventory, the contractor conducted a detailed analysis of U.S. production and import activity using data available from the EPA Chemical Data Reporting (CDR) program, and the manufacturing, processing, and waste management trends of OFR substances from the Toxic Release Inventory (TRI), as reported by industrial and federal facilities.

To determine whether individual OFR chemicals are used in consumer and/or children's products the contractor reviewed information available from the EPA's CDR and the Interstate Chemicals Clearinghouse High Priority Chemicals Data System (HPCDS). European data on OFR substances in products could not be reviewed in entirety in time for the publication of the report.

In addition, the contractor made efforts to identify OFR chemicals on several chemical business to business (B2B) or e-Commerce sites, using automated techniques to "scrape" data on OFRs from these sites. From Buyersguide.com and Chemnet.com, the contractor obtained the identity, country, and website of OFR suppliers. From Alibaba.com, they obtained the name and website of the OFR suppliers, as well as some data on quantities available and pricing.

4.4. Literature Survey

The OFR literature survey was intended to gather readily available toxicity, exposure, and risk information to characterize the types and amounts of data available for chemicals (and analogs) within a class. CPSC staff defined data sources for the literature survey effort as toxicity, exposure, and chemistry databases; completed toxicity, exposure, or risk assessments; and completed literature reviews. Sources identified in the literature survey were screened to confirm utility and identify the type of data, but the actual data were not evaluated or extracted.

Detailed descriptions of the literature survey approach and process are found in the Literature Survey Guide and accompanying documentation. These documents were developed by University of Cincinnati (UC) Risk Science Center staff as part of work performed under a CPSC-sponsored contract (UC, 2022a; UC, 2022b). Development of the evidence maps followed a multilevel process to screen data sources initially identified in a defined search.

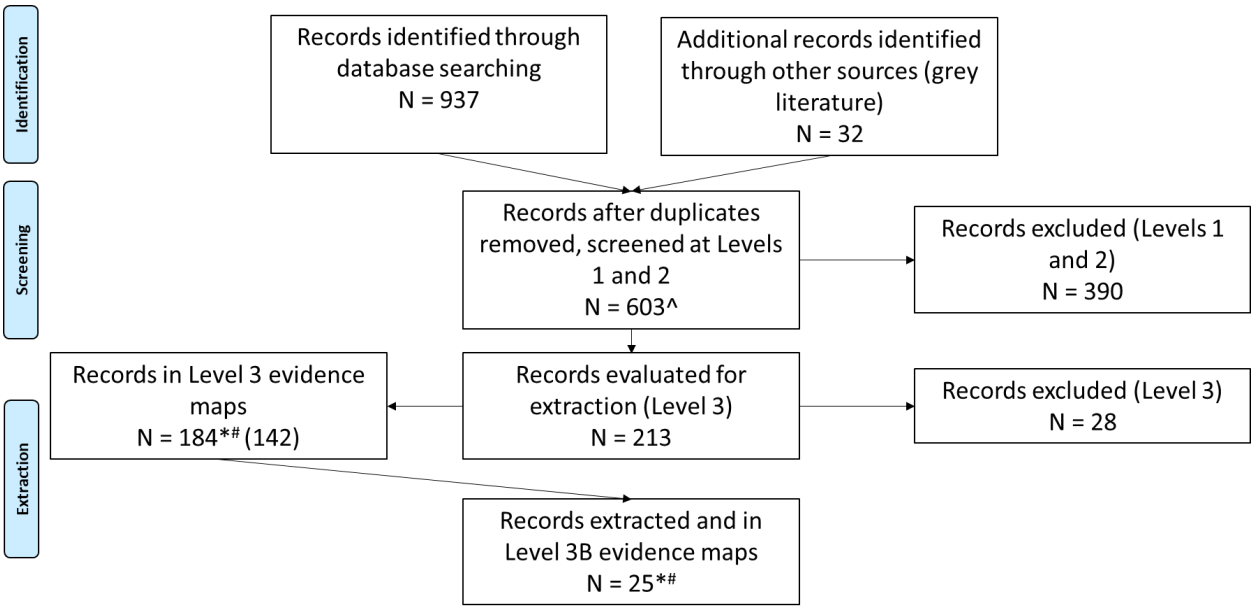
Briefly, for peer-reviewed and gray literature, **Level 1** screening was used to confirm that the reference might contain information about at least one OFR chemical and that the reference

was relevant to the PECO statement.[10] **Level 2** screening identified the OFR subclasses included in each reference and tagged the references for the types of data (hazard, exposure, risk). **Level 3** identified the specific OFR or analog chemicals in each reference and extracted more specific information about the types of hazard data, exposure data, or risk assessment information presented for each chemical. Finally, **Level 3B** tagging was performed on a subset of toxicity assessments, toxicity literature reviews, risk assessments, and exposure literature reviews selected from Level 3 to identify even more specific information for the chemicals in these references.

Similarly, data from databases were tagged for type of data using a database logic developed to provide consistency across different data sources. Finally, the tagged information was organized into evidence maps by OFR subclass and specific chemicals. Figure 4-1 shows the numbers of records initially identified and the number of records screened or extracted at each level.

[10] PECO refers to population (P), exposure (E), comparator (C), and outcomes (O) of interest, and generally describes the scope of a literature search and subsequent analyses.

Figure 4-1. Literature Flow Diagram



Notes:
^Removal of duplicates within the class, and between PHBAFs and previous classes.
*PHBAF evidence maps contain additional references uploaded with Class 1 PHOPs. Number in parentheses is the number of references identified by searching for the PHBAF class only, excluding the references identified by searching for PHBAFs.
#One reference that was manually identified outside of Distiller was included in Level 3B extraction and evidence maps.

5. Scoping for PHBAFs

5.1. PHBAF Subclass Chemistry

The PHBAF subclass consists of halogenated functionalized bisphenol A derivatives for which the halogens may be either chlorine (-Cl) or bromine (-Br) groups. A bisphenol S compound was included in this class due to its structural similarity. The chemical structures can be described as two halogenated phenols bridged by either a methylene ($-CR_2$, $R=CH_3$) or sulfonyl ($-SO_2$) group in the case of the bisphenol S derivative. The hydroxyl group of these bisphenol compounds may also be further functionalized by aliphatic chains.

Table 5-1 lists 14 individual chemicals in the PHBAF subclass.

Table 5-1. List of Chemicals in PHBAF Subclass

	CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
1	21850-44-2	Tetrabromobisphenol A-bis(2,3-dibromopropyl ether)	TBBPA-DBPE	CC(C)(C1=CC(Br)=C(OCC(Br)CBr)C(Br)=C1)C1=CC(Br)=C(OCC(Br)CBr)C(Br)=C1
2	25327-89-3	Tetrabromobisphenol A diallyl ether	TBBPA-BAE	CC(C)(C1=CC(Br)=C(OCC=C)C(Br)=C1)C1=CC(Br)=C(OCC=C)C(Br)=C1
3	29426-78-6	4,4'-(propane-2,2-diyl)bis(2-bromophenol) or 3,3'-Dibromobisphenol A	NA	CC(C)(C1=CC(=C(C=C1)O)Br)C2=CC(=C(C=C2)O)Br
4	3072-84-2	2,2'-[(1-Methylethylidene)bis[(2,6-dibromo-4,1-phenylene)oxymethylene]]bis[oxirane]	TBBPA-BGE	CC(C)(C1=CC(Br)=C(OCC2CO2)C(Br)=C1)C1=CC(Br)=C(OCC2CO2)C(Br)=C1
5	33798-02-6	Phenol, 4,4'-(1-methylethylidene)bis[2,6-dibromo-, 1,1'-diacetate	TBBPA-BOAC	CC(=O)OC1=C(Br)C=C(C=C1Br)C(C)(C)C1=CC(Br)=C(OC(C)=O)C(Br)=C1
6	37419-42-4	3,3',5,5'-Tetrabromobisphenol A bispropionate	TBBPA-BP	CCC(=O)OC1=C(Br)C=C(C=C1Br)C(C)(C)C1=CC(Br)=C(OC(=O)CC)C(Br)=C1
7	37853-61-5	Tetrabromobisphenol A dimethyl ether	TBBPA-BME	COC1=C(Br)C=C(C=C1Br)C(C)(C)C1=CC(Br)=C(OC)C(Br)=C1
8	4162-45-2	Tetrabromobisphenol A-bis(2-hydroxyethyl) ether	TBBPA-BHEE	CC(C)(C1=CC(Br)=C(OCCO)C(Br)=C1)C1=CC(Br)=C(OCCO)C(Br)=C1
9	55205-38-4	(Propane-2,2-diyl)bis(2,6-dibromo-4,1-phenylene) diprop-2-enoate	TBBPS-BA	CC(C)(C1=CC(Br)=C(OC(=O)C=C)C(Br)=C1)C1=CC(Br)=C(OC(=O)C=C)C(Br)=C1
10	66710-97-2	Bis(p-acryloxyethoxy)tetrabromobisphenol A	TBBPA-BHEEBA	CC(C)(C1=CC(Br)=C(OCCOC(=O)C=C)C(Br)=C1)C1=CC(Br)=C(OCCOC(=O)C=C)C(Br)=C1
11	70156-79-5	1,1'-sulfonylbis(3,5-dibromo-4-methoxybenzene)	TBBPS-BME	COC1=C(Br)C=C(C=C1Br)S(=O)(=O)C1=CC(Br)=C(OC)C(Br)=C1
12	79-94-7	3,3',5,5'-Tetrabromobisphenol A	TBBPA	CC(C)(C1=CC(Br)=C(O)C(Br)=C1)C1=CC(Br)=C(O)C(Br)=C1
13	79-95-8	2,2',6,6'-Tetrachlorobisphenol A	TCBPA	CC(C)(C1=CC(Cl)=C(O)C(Cl)=C1)C1=CC(Cl)=C(O)C(Cl)=C1
14	97416-84-7	1,1'-(Isopropylidene)bis(3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)benzene)	NA	CC(Br)(CBr)COC1=C(Br)C=C(C=C1Br)C(C)(C)C1=CC(Br)=C(OCC(C)(Br)CBr)C(Br)=C1

SMILES = simplified molecular-input line-entry system. NA = not available or not found.

5.1.1. Physicochemical Property Summaries

The information collected to date led CPSC staff to find that experimental physicochemical data on PHBAF chemicals are limited. Four PHBAF subclass members have experimental data and all 14 PHBAF members have predicted data. Well-studied chemicals in this subclass include 3,3',5,5'-tetrabromobisphenol A (TBBPA, CAS RN 79-94-7), 2,2'-[(1-methylethylidene)bis[(2,6-dibromo-4,1-phenylene)oxymethylene]]bis[oxirane] (TBBPA-BGE, CAS RN 3072-84-2) and tetrabromobisphenol A-bis(2,3-dibromopropyl ether) (TBBPA-DBPE, CAS RN 21850-44-2). From this data set, studied PHBAFs have vapor pressures ranging from $4.68E^{-8}$ to $2.18E^{-4}$ mm Hg. Data show water solubility values ranging from $1.53E^{-10}$ to $2.32E^{-6}$ mol/L. The octanol/water partition coefficient (K_{ow}) values, which are commonly expressed as log K_{ow}, range from 4.75 to 7.2. A detailed list of experimental and predicted physicochemical values are located in the supplemental file for chemical descriptors and physicochemical properties (Supplemental File 3: Chemical Descriptors and Physicochemical Properties for PHBAF Class and Analogs) (see Appendix: Supporting Files).

5.2. Market and Use Summary for PHBAFs

The OFR Market and Use Report, completed in March 2022, includes 14 PHBAF chemicals.

- All PHBAF chemicals had market and use information (zero PHBAF chemicals had no market and use information).
- According to EPA data, six PHBAF chemicals were identified to be on the EPA's TSCA chemical substance (active) inventory, three PHBAF chemicals were identified on the TSCA (inactive) inventory, three were on the CDR, and one was on the TRI program list.
- One PHBAF chemical was identified in the Interstate Chemicals Clearinghouse (IC2) HPCDS.
- Twelve PHBAF chemicals were identified in the targeted literature search.
- Thirteen PHBAF chemicals had patent data.

5.2.1. PHBAFs Used in Commerce

The Market and Use Report summarizes data from a variety of sources, including U.S. and international chemical registries, scientific literature, patents, and chemical databases. To determine whether individual OFRs are currently in commerce, have been used in the past, or may be used in the future, these registries, patent data, and literature were reviewed in detail under a CPSC-sponsored contract and data were compiled from four main types of sources. Chemicals that have been in commerce appear on the (1) TSCA inventory, (2) international inventories, (3) in literature, or (4) in patent data. Table 5-2 lists the 14 PHBAFs that are known to be or have been used in commerce, according to data available from these sources.

Among the 14 PHBAF chemicals used in commerce, 9 can be found on the TSCA inventory. Six of these chemicals are on the TSCA active inventory and three PHBAFs are on the TSCA inactive inventory. In Table 5-2, PHBAF chemicals found on the TSCA inventory are identified as "Active" or "Inactive," accordingly.

Five other international registries were reviewed: EU REACH (2021), CANADA DSL (2021), MEXICO INSQ (2009), JAPAN CSCL (2021), AND CHINA IECSC (2013).[11] Nine PHBAF chemicals appear on one or more of these international inventories. In Table 5-2, the number of international registries for the identified PHBAF chemicals is listed in the "International Inventories" column.

Twelve PHBAF chemicals were identified in the literature through a targeted literature search.[12] In Table 5-2, the numeric value listed in the "Literature Cites" column is the number of sources from the targeted literature search that referenced the chemical.

Thirteen PHBAF chemicals were mentioned in patents. The total count of patents is provided for each chemical in Table 5-2, returned from a search of the associated Compound Identifier (CID) in PubChem.

Table 5-2. PHBAF Chemicals Used in Commerce

CAS RN	Chemical Name	TSCA	International Inventories	Literature Cites	Patents
21850-44-2	Tetrabromobisphenol A-bis(2,3-dibromopropyl ether)	Active	2	13	3,058
25327-89-3	Tetrabromobisphenol A diallyl ether	Active	3	8	1,619
29426-78-6	4,4'-(propane-2,2-diyl)bis(2-bromophenol)	Not found	Not found	0	9,486
3072-84-2	2,2'-[(1-Methylethylidene)bis[(2,6-dibromo-4,1-phenylene)oxymethylene]]bis[oxirane]	Active	2	2	151
33798-02-6	Phenol, 4,4'-(1-methylethylidene)bis[2,6-dibromo-, 1,1'-diacetate	Inactive	Not found	1	9
37419-42-4	3,3',5,5'-Tetrabromobisphenol A bispropionate	Not found	Not found	1	0
37853-61-5	Tetrabromobisphenol A dimethyl ether	Active	1	3	56
4162-45-2	Tetrabromobisphenol A bis(2-hydroxyethyl) ether	Active	2	3	535
55205-38-4	(Propane-2,2-diyl)bis(2,6-dibromo-4,1-phenylene) diprop-2-enoate	Not found	Not found	1	1,637

[11] EU REACH = European Union Registration, Evaluation, Authorisation, and Restriction of Chemicals; INSQ = Inventario Nacional de Sustancias Químicas; CSCL = Chemical Substances Control Law; IECSC = Inventory of Existing Chemical Substances Produced or Imported in China.
[12] For additional detail on the methodology used for the targeted literature search, see Section 4.3.1, Targeted Literature Search, in this scope document.

CAS RN	Chemical Name	TSCA	International Inventories	Literature Cites	Patents
66710-97-2	Bis(p-acryloxyethoxy)tetrabromobisphenol A	Inactive	1	1	74
70156-79-5	1,1'-sulfonylbis(3,5-dibromo-4-methoxybenzene)	Not found	Not found	1	4
79-94-7	3,3',5,5'-Tetrabromobisphenol A	Active	4	42	81,973
79-95-8	2,2',6,6'-Tetrachlorobisphenol A	Inactive	1	0	25,180
97416-84-7	1,1'-(Isopropylidene)bis(3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)benzene)	Not found	2	1	31

Table 5-2 shows that information indicating commercially used PHBAF chemicals is available from thousands of patents, numerous literature sources, and multiple chemical inventories.

5.2.2. PHBAFs Used in Consumer Products

The Market and Use Report identified the use of PHBAFs in consumer products, including children's products. To determine whether individual OFR chemicals are used in consumer and/or children's products, a CPSC-sponsored contractor reviewed the information available from the EPA's CDR,[13] the European Chemicals Agency's (ECHA) Substances of Concern in articles as such or in complex objects (Products) (SCIP) database, and the IC2's HPCDS. Data on the uses and applications of PHBAF chemicals were also found in the literature.

Targeted Literature Search. In the literature, several sources report the results of product testing, and these indicate PHBAFs have been found in a variety of consumer and/or children's products (product reported concentrations are in parentheses), such as:

- Hard plastic toys (0% to 21.3%)
- Soft plastic toys (0% to 3.7%)

The following PHBAF chemicals were identified from the targeted literature search to have been used in consumer and children's products, and example uses are provided below:

CAS No. 79-94-7: durable infant or toddler products, toys, childcare articles or other children's products other than car seats, mattresses and mattress pads, plastic products, all electric/electronic equipment, E-waste, adaptors, heat sealers, powerboards, LCD TVs, TVs, plastic ornaments, electrical adaptors, televisions, decorative items, routers, plastics, resin, food contact articles, textiles, curtains, carpets, printers, tv housings, expanded polystyrene, extruded polystyrene foam, construction materials, and paper.

CAS No. 4162-45-2. engineering polymers, epoxy resins, thermoset and thermoplastic polyesters, polyurethane, laminates for electronic circuit boards, and adhesives and coatings.

[13] Data from the review of EPA's CDR for consumer products was generally incomplete, especially for children's products, and therefore are not summarized below; however, they are available in Section 3.2.5.1 in Volume I of the Market and Use Report.

CAS No. 25327-89-3: expanded polystyrene and polystyrene foams, adhesive pipes, water barriers, kitchen hoods, curtains, electronic equipment (TV, audio, video) and PC monitors, polyolefin and styrene resins, and high-impact polystyrene.

CAS No. 4162-45-2: engineering polymers, epoxy resins, thermoset and thermoplastic polyesters, polyurethane, laminates for electronic circuit boards, and adhesives and coatings.

HPCDS. Using the HPCDS reporting tool, private industry reports the use of chemicals of concern in products intended for use by children that are sold in select states.[14] From 2012 to 2020, 1,093 reports were submitted to HPCDS identifying the use of OFR chemicals from seven subclasses in children's products sold in two U.S. states, Washington and Oregon. Twenty-three percent, or 246 reports, documented the use of PHBAF chemicals in children's products.

Table 5-3 shows information on the total report count, the uses, and concentration of a common PHBAF chemical (tetrabromobisphenol A, 79-94-7) reported to be used in children's products. Of the 246 reported uses of PHBAFs in children's products, all were for use of tetrabromobisphenol A. Approximately one-third of the reported uses of the substance (84 reports) were for use as a chemical flame retardant. Of the 246 reported uses of tetrabromobisphenol A in children's products, most uses of the substance were reportedly used in trace amounts, although 33 reports identified the use of the substance in children's products in concentrations greater than 1,000 ppm (0.1%), a threshold CPSC staff considers above the level of contaminant.[15] There were 12 reported uses of tetrabromobisphenol A in concentrations greater than 0.1% that were expressly for use as a chemical flame retardant in a children's product.

Table 5-3. Number of Children's Products with Reported Use as Flame Retardants for Select PHBAF Chemical

PHBAF	Total Report Count	Flame Retardant Use	Concentration >0.1%	Concentration >0.1% + FR Use
79-94-7	246	84	33	12

Source: HPCDS, Interstate Chemicals Clearinghouse.

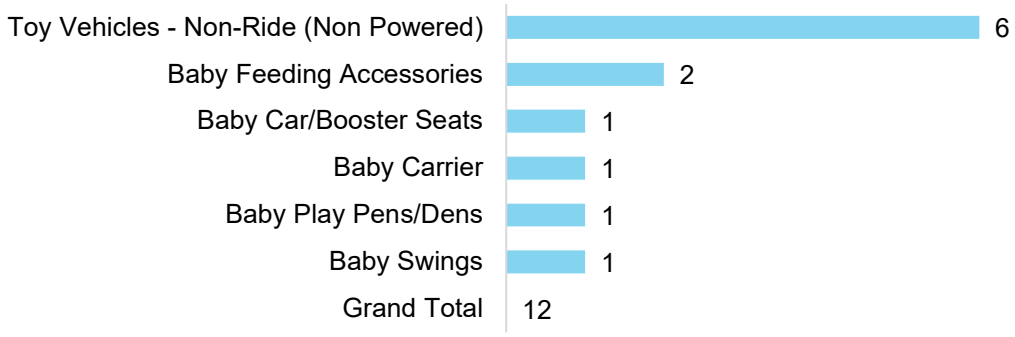
As shown in Figure 5-1, the 12 reported applications for which tetrabromobisphenol A is used as a chemical flame retardant (in concentrations greater than 0.1%) were children's (non-powered) non-ride toy vehicles, baby feeding accessories, baby car and booster seats, baby carriers,

[14] At this time, CPSC staff is unable to determine if information reported to the HPCDS for Washington and Oregon are representative. Presumably, the number of reports would go up substantially if information for all 50 states were available; however, it is not known whether the chemicals identified and types of children's products would also change.

[15] This amount corresponds with information on candidate list substances in articles in which importers and producers have to submit notification to the European Chemicals Agency (ECHA) if a substance is present in a concentration above 0.1% weight by weight (Introduction to Information on Candidate List substances in articles ECHA [echa.europa.eu]). CPSC staff rationale is that it should consider 0.1% or below to represent a contamination level given that concentrations of these chemicals when used intentionally as flame retardants are typically much higher.

baby play pens and dens, and baby swings. (See Exhibit 3-28 in the Market and Use Report, Volume 1.)

Figure 5-1. Children's Products That Contain PHBAF Chemical Flame Retardants



Source: HPCDS, Interstate Chemicals Clearinghouse.

Among children's products identified to contain PHBAF chemical FRs in a concentration greater than 0.1%, tetrabromobisphenol A, also known as TBBPA, is reportedly found in synthetic polymers (e.g., synthetic rubber, plastics, foams) and in textiles (e.g., synthetic fibers and blends), in concentrations greater than 1,000 ppm. (See Table 5-4.)

Table 5-4. Component Parts That Contain PHBAF Chemicals, at a Concentration Equal to or Greater than 1,000 ppm, when Used as Flame Retardant in a Children's Product (2012–2020)

Chemical (CAS RN)	Chemical Name	Synthetic Polymers (Synthetic Rubber, Plastics, Foams, Etc.)	Textiles (Synthetic Fibers and Blends)
79-94-7	Tetrabromobisphenol A	X	X

SCIP. ECHA maintains a database of information through the REACH regulation, which was enacted in 2007 to improve the protection of human health from risks posed by chemicals. REACH applies to consumer products as well as to the chemicals industry. The REACH regulation requires suppliers of articles (products) containing potentially hazardous chemicals, including OFRs, to communicate down the supply chain and to consumers sufficient information to allow for the safe use of those products that contain them. Any supplier of an article containing a substance of very high concern (SVHC) in a concentration above 0.1% weight by weight (w/w) on the EU market is required to submit information on that article to ECHA. This information is commonly referred to as a "SCIP notification." From data available from the European Union, SCIP notifications have supported the development of the SCIP database.

The SCIP database is an important tool of the REACH framework and helps ensure that information regarding the use of hazardous substances in products is more readily and efficiently shared within the supply chain, and that certain information regarding the use of hazardous substances in products is also available to the public.

Table 5-5 shows that one PHBAF chemical was included in the SCIP database.[16] (See Exhibit 3-30 in the Market and Use Report, Volume 1.)

Table 5-5. PHBAF Chemicals Included in SCIP Database

CAS RN	Substance Name	EC No.	Number of Search Results Returned
79-94-7	Tetrabromobisphenol A	201-236-9	154,023

As of May 2023, there were 154,023 search results for tetrabromobisphenol A (CAS RN 79-94-7) in the SCIP database. Articles that contain this candidate list substance can be found in over 20 article categories that can be used to help identify articles based on function and use. According to SCIP data, tetrabromobisphenol A can be found in vehicles, machinery and appliances, and optical instruments. However, because SCIP data were first released in September 2021, they could not be reviewed in time for publication of the Market and Use Report.

CDR. According to data available from the EPA's CDR, PHBAF chemicals have been used in a variety of product use categories for many years (see Table 5-6.) This table presents both commercial and consumer product uses of PHBAF chemicals because CPSC needs to know the range of the product uses for these chemicals during the scoping phase.[17]

EPA changed the names of some product use categories between 2006 and 2012, and again in 2016, and so Table 5-6 presents the names of product use categories of PHBAF chemicals in the three reporting periods.[18] To handle small changes in product use category names over these periods, staff used a more generic or general name to be inclusive. The designated general product use category names help maintain consistency over the period displayed in the table below without distorting product use.

According to the CDR, the most common uses of PHBAF chemicals are in electrical and electronic products, rubber and plastic products, and other products not identified, although PHBAFs are reported to be used in a variety of other products as well.

[16] There were no PHBAF chemicals included in the SCIP database when the Market and Use Report was finalized in March 2022. However, as of April 2023, an updated search of the SCIP database reveals multiple reports of Tetrabromobisphenol A (CAS No. 79-94-7).
[17] In the global economy, supply chains are complex, and reporters to the CDR do not know (and cannot reasonably ascertain) the end use of a product. Therefore, CPSC is reviewing all product use categories of OFR chemicals reported to the CDR, but may exclude certain categories later, if there is sufficient evidence showing that these chemical substances can be found exclusively in commercial products.
[18] For the 2006, 2012, and 2016 reporting periods, chemical-specific product use reporting was only required for the principal reporting year (PRY), the latest completed calendar year preceding the submission period. Therefore, 2006 data are from PRY 2005, 2012 data are from PRY 2011, and 2016 data from PRY 2015.

Table 5-6. Report Counts of Commercial and Consumer Product Uses of PHBAF Chemicals

Product Use Category	2006	2012	2016	Total
Building/construction materials not covered elsewhere	NR	NR	1	**1**
Product description, not identified	3	1	NR	**4**
Rubber and plastic products	NR	3	2	**5**
Electrical and electronic products	1	3	4	**8**
Industrial manufacturing	NR	NR	1	**1**
Grand Total	**4**	**7**	**8**	**19**

Notes: Data listed as "Product description not identified" may be interpreted as one of any of the other product categories reported for PHBAFs, generally. NR = not reported or not available.

In addition, the CDR provides an opportunity for firms that report the use of a chemical substance to identify if the substance could be used in children's products. However, the CDR should not be considered a complete source for identifying the use of OFR chemical substances in children's products.[19] In 2006, the use of PHBAF chemicals in children's products was considered by reporting firms to be confidential business information (CBI) and the product category use of PHBAF chemicals was also considered CBI. In 2012, the use of PHBAF chemicals in children's products was considered by reporting firms to be not known or reasonably ascertainable (NKRA) and the product category use of PHBAF chemicals was also considered NKRA. In 2016, the use of PHBAF chemicals in children's products was considered by reporting firms to be NKRA for use in plastic and rubber products.

5.2.3. Regulatory History and Trends for PHBAFs

OFRs have received considerable regulatory attention from governmental jurisdictions in the United States and around the world; however, the scope and applicability of these regulatory actions varies significantly. This section discusses legislative action taken in the United States at the state level and in Europe through ECHA.

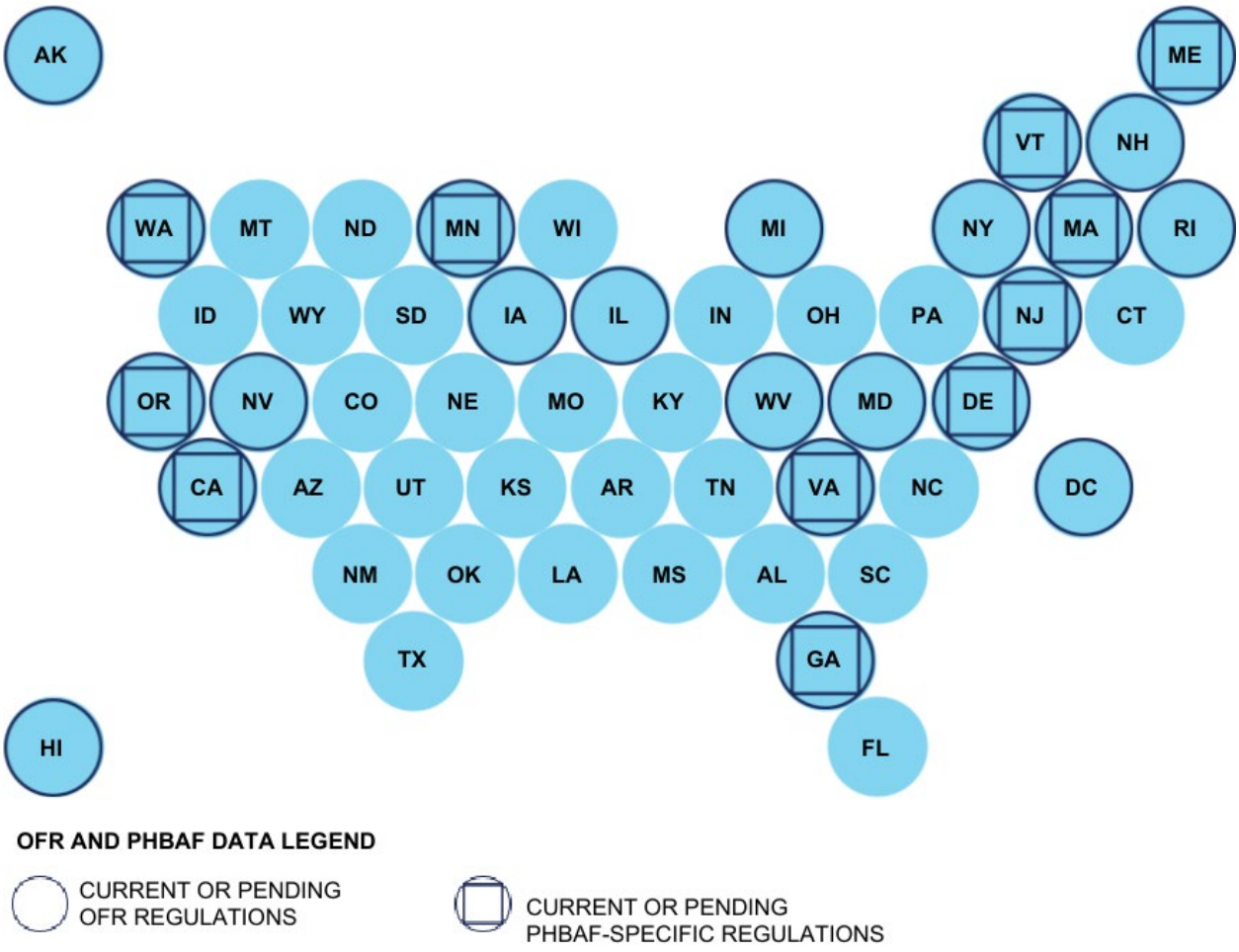
The Market and Use Report provides greater detail of legislative action taken in the United States, as well as action taken by other nations. Volume 2, Appendix R of the Market and Use Report provides detailed fact sheets describing specific pieces of legislation enacted or under consideration since 1986 in 21 U.S. states and the District of Columbia, at the U.S. federal level, and by Canada, the EU, and Japan.[20]

According to the Market and Use Report, 22 states and the District of Columbia have current or pending OFR chemical regulations. State regulation of OFRs has tended to focus primarily on

[19] The CDR rule provides reporting exemptions for chemical substances in articles, byproducts, impurities, non-isolated intermediates, certain polymers, research and development, and those produced by small manufacturers and small importers. 40 C.F.R. §§ 704.5 and 711.6. The CDR rule also exempts chemical substances manufactured in quantities of less than 2,500 pounds. Id. at § 711.15.
[20] As part of work performed under the CPSC-sponsored contract, CPSC staff also sought to identify legislation developed in China related to OFRs. The literature review suggests China imposes some restrictions on OFRs, which is discussed more generally in Section 4.1.3 of Volume 1 of the Market and Use Report.

the use of these chemicals in children's products, upholstered furniture, and mattresses. (See Market and Use Report Volume 1, section 4.1.2.4 Summary of U.S. Regulatory Trends.) Among areas that have proposed or enacted regulation of the use of OFRs, 11 states have proposed or enacted regulation of the use of PHBAFs specifically. In the map below (Figure 5-2), states that regulate OFRs or have pending regulations are shown with circles, and states that regulate PHBAFs specifically or have pending PHBAF-specific regulations are shown with a square within the circle. For more information on the state regulation of OFRs and PHBAFs, see Volume 2 of the Market and Use Report, Appendix R.

Figure 5-2. U.S. States That Regulate the Use of OFR and PHBAF Chemical Flame Retardants



The sharing of data reported to states helps to improve the effectiveness of enacted legislation on potentially hazardous OFR chemicals and to address information asymmetries in the market. Increasingly, state legislation compels reporting and allows for reciprocal data-sharing

agreements with trade associations, the IC2, or other independent third parties. Reported data are also shared with the public. According to data compiled in the Market and Use Report (see Appendix R of Volume 2), eight states and the District of Columbia have reporting or data-sharing requirements for OFR chemicals.

5.3. Literature Survey Results: Evidence Maps of Toxicity Data

The toxicity evidence map descriptions below are high-level observations of the Level 2, 3, and 3B literature surveys in the designated spreadsheet files.[21] The database counts indicate either the number of sources within the database (if available) or the number of entries in the database (if no information on source is available) after attempts were made to remove duplicates. The unit for PDF counts is the individual PDF file. Level 3B tagging was performed on a subset of 25 toxicity assessments, toxicity literature reviews, and risk assessments selected from Level 3 to identify even more specific information for the chemicals in these references. Note that most of the Level 3B data are from database data, and only a subset of the PDF data sources is tagged at Level 3B.

Review of the Level 2, 3, and 3B summaries described below indicate that TBBPA is the most data rich PHBAF member for toxicity. It had the highest number of toxicity data sources in each category, and it had the most representation across exposure categories for database and PDF reviews. The analogs had QSAR/Read-Across data and assessments but no experimental data.

5.3.1. Summary of Level 2

The "Integrated" tab contains summed Level 2 toxicity data counts across PDF and database data.[22] At Level 2, the unit for database counts is the database with relevant data across 16 toxicity databases searched. The unit for PDF counts is the individual PDF file. Each database or PDF could contain more than one data point per chemical. Attempts were made to remove duplicates, but some data sources may have been counted more than once.

The literature survey identified integrated data sources (sum of databases and PDFs) for all 14PHBAF members and for all 16 analogs. The PHBAF members with the most data sources were TBBPA, 2,2',6,6'-tetrachlorobisphenol A, and TBBPA-DBPE. Each of the 16 analogs had one to three toxicity data sources at Level 2. Table 57 summarizes how many PHBAF members and analogs had different degrees of data source abundance.

[21] See evidence map files on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022.
[22] See evidence map file "PHBAF Level 2 Evidence Maps 12.2.22, Tab: Integrated" on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022.

Table 5-7. Distribution of Toxicity Data Source Abundance Levels at Level 2

Distribution of Number of Data Sources Available for Each Chemical	Number of Chemicals with Level 2 Toxicity Data Sources	
	PHBAF Chemicals (n = 14)	Analog Chemicals (n = 16)
21+	1	0
6–20	5	0
1–5	8	16
0	0	0

5.3.2. Summary of Levels 3 and 3B

The "TOX_Integrated" tabs from each file contain Level 3 and Level 3B toxicity data counts across all toxicity databases and PDFs.[23] The Level 3B tabs were divided into A, B, and C to keep the spreadsheets manageable. Integrated Level 3B counts report the sum of data sources from databases and a selected PDFs (i.e., not all PDFs identified at Level 3 were reviewed at Level 3B). The integrated counts indicate the number of data sources per chemical from databases and PDFs identified and classified into seven toxicity data type categories. At Level 3B, reviewers tagged the data sources from each category with subcategories to provide additional details of specific data types. Table 5-8 and Table 5-9 summarize how many PHBAF members and analogs had different degrees of Level 3 toxicity data source abundance.

Table 5-8. Distribution of Toxicity Data Source Abundance Levels at Level 3 – Chemicals

Distribution of Number of Data Sources Available for Each Chemical	Number of Chemicals with Level 3 Toxicity Data Sources						
	PHBAF Chemicals (n = 14)						
	Animal Toxicity or Accepted Alternative	Human Toxicity	Human, Animal, or Modeled Toxicokinetics (ADME)	Experimental Mechanistic	QSAR, Read-Across, Analog	Qualitative Hazard Characterization	Quantitative Hazard Characterization
21+	3	0	1	5	12	1	3
6–20	4	1	5	1	2	4	4
1–5	3	1	5	2	0	5	2
0	4	12	3	6	0	4	5

[23] See evidence map file: "PHBAF Level 3 Evidence Maps 12.2.22, Tab: TOX Integrated" and "PHBAF Level 3B Evidence Maps 12.2.22, Tab: TOX Integrated" on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022.

Animal Toxicity or Accepted Alternative data sources were available for 10 PHBAF members and no analogs at each Level 3 and 3B Reviews. Level 3B reviews provided additional detail for these counts across nine subcategories: Acute Toxicity, Systemic or Repeated Dose Toxicity, Neurotoxicity, Carcinogenicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental, Irritation, Sensitization, and Endocrine Disruption. CPSC staff observed the following:

- PHBAF members TBBPA and TBBPA-DBPE had data sources in all subcategories and had the highest total counts of data sources across subcategories.
- PHBAF member 1,1'-(Isopropylidene)bis(3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)benzene) had data sources for all subcategories except Neurotoxicity, Carcinogenicity, and Endocrine Disruption.
- Systemic or Repeated Dose Toxicity, Mutagenicity/Genotoxicity, and Irritation each had eight PHBAF members; these the subcategories had data sources for the most PHBAF members.
- Four PHBAF members [tetrabromobisphenol A dimethyl ether; 4,4'-(propane-2,2-diyl)bis(2-bromophenol); 3,3',5,5'-tetrabromobisphenol A bispropionate; and (propane-2,2-diyl)bis(2,6-dibromo-4,1-phenylene) diprop-2-enoate] had no animal toxicity data.

Table 5-9. Distribution of Toxicity Data Source Abundance Levels at Level 3 – Analogs

Distribution of Number of Data Sources Available for Each Chemical	Number of Chemicals with Level 3 Toxicity Data Sources PHBAF Analogs (n = 16)						
	Animal Toxicity or Accepted Alternative	Human Toxicity	Human, Animal, or Modeled Toxicokinetics (ADME)	Experimental Mechanistic	QSAR, Read-Across, Analog	Qualitative Hazard Characterization	Quantitative Hazard Characterization
21+	0	0	0	0	6	0	0
6–20	0	0	0	1	0	0	0
1–5	0	0	6	1	10	0	0
0	16	16	10	14	0	16	16

Human Toxicity data sources were available for two PHBAF members and no analogs at Level 3 review. One PHBAF member and no analogs had data available at Level 3B review. Level 3B reviews provided additional detail across the same nine subcategories used for *Animal Toxicity or Accepted Alternative* above CPSC staff observed the following:

- TBBPA had three data sources in each of the Neurotoxicity, Reproductive Toxicity/Developmental, Sensitization, and Endocrine Disruption subcategories.

- TBBPA had one data source in each of the Mutagenicity/Genotoxicity and Irritation subcategories.
- *Human Toxicity* is the category with the least overall data availability.

Human, Animal, or Modeled Toxicokinetics (ADME [absorption, distribution, metabolism, and excretion]) data sources were available for 11 PHBAF members and six analogs at Level 3 review. Eleven PHBAF members and six analogs had data in the databases and selected PDFs at Level 3B review. Level 3B reviews provided additional detail for these counts across seven subcategories: Human Absorption, Distribution, Excretion; Animal Absorption, Distribution, Excretion; Human Metabolism; Animal Metabolism; In Vitro; or Chemical- or Class-Specific physiologically based pharmacokinetic (PBPK) Model; and Chemical- or Class-Specific QSAR for an ADME Parameter. CPSC staff observed the following:

- PHBAF member TBBPA had data sources in all subcategories and had the highest total counts of data sources across subcategories.
- The subcategory with the most data sources and for the most chemicals was Chemical- or Class-Specific QSAR for an ADME Parameter, with data sources identified for 11 PHBAF members and six analogs (the only analog data sources in this category).

Experimental Mechanistic data sources were available for nine PHBAF members and two analogs at Level 3 review. Five PHBAF members and no analogs had data in the databases and selected PDFs at Level 3B review.[24] This category had two subcategories at Level 3B review separating those data sources that make a connection to a mode of action (MOA) and a potential health effect from those that do not.[25] CPSC staff observed the following:

- Three PHBAF members had data sources in both subcategories. These include TBBPA, TBBPA-BAE, and 2,2',6,6'-Tetrachlorobisphenol A. Some of these hit counts were large with hundreds or thousands of data sources per chemical per subcategory.
- The remaining two PHBAF members with data sources in this category (TBBPA-BHEE and TBBPA-DBPE) had hits only in the -Study Makes Connection to MOS and Potential Health Effect- subcategory.

QSAR, Read-Across, Analog data sources were available for all 14 PHBAF members and all 16 analogs at Level 3 review, and the same counts were reported at Level 3B review. Level 3B reviews provided additional detail across the same nine subcategories used for *Animal Toxicity or Accepted Alternative* above. CPSC staff observed the following:

- At least one data source was available in all subcategories for five PHBAF members. These include TBBPA, TBBPA-DBPE, TBBPA-BAE, TBBPA-BHEE, and 1,1'-(Isopropylidene)bis(3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)benzene).

[24] See "TOX_DB" and "TOX_PDF" tabs of evidence map file on the CPSC Organohalogen Flame Retardant Chemicals Assessment website. The 3B data counts for Experimental Mechanistic data are presented only in the "TOX_DB" and "TOX_PDF" tabs and not in the "TOX_Integrated" tab, because PubChem Bioassay data did not contain enough information to distinguish between the Level 3B tags for mechanistic data.
[25] Many database sources could not be tagged for Level 3B because it was not clear whether a connection was made to MOA.

- Subcategories Mutagenicity/Genotoxicity and Endocrine Disruption had data for all chemicals in this subclass including members and analogs.
- Subcategories Acute Toxicity and Reproductive Toxicity/Developmental Toxicity had data for all chemicals in this subclass except PHBAF member 4,4'-(propane-2,2-diyl)bis(2-bromophenol).
- The Endocrine Disruption subcategory had the highest numbers of hits per chemical including members and analogs.
- Five analogs had data in all subcategories except Neurotoxicity.

Qualitative Hazard Characterization data sources were available for 10 PHBAF members and two analogs at Level 3 review, and the same counts were reported at Level 3B review. This category was separated into the same nine subcategories used for Animal Toxicity of Accepted Alternative above for Level 3B review. CPSC staff observed the following:

- PHBAF members TBBPA, TBBPA-DBPE, and 1,1'-(Isopropylidene)bis(3,5-dibromo-4-(2,3-dibromo-2-methylpropoxy)benzene) had data sources for each of the nine subcategories.
- PHBAF member TBBPA-BHEE had data sources in all subcategories except Endocrine Disruption.
- The subcategory with data for the most PHBAF members was Irritation (eight chemicals) followed by Acute Toxicity and Sensitization (seven chemicals each).
- Two analogs had data in the Endocrine Disruption subcategory only. All other analogs had no data for this category.

Quantitative Hazard Characterization data sources were available for nine PHBAF members and no analogs at Level 3 review, and the same counts were reported at Level 3B review. At Level 3B review, this category was further divided into seven subcategories: Acute Toxicity, Systemic or Repeated Dose Toxicity, Neurotoxicity, Carcinogenicity, Reproductive Toxicity/Developmental, Sensitization, and Endocrine Disruption.

- PHBAF member TBBPA had data in all subcategories except Sensitization and had the highest numbers of data sources across the remaining subcategories.
- None of the chemicals in this subclass had data for Sensitization.
- The subcategory with the most chemicals with data was Acute Toxicity (eight members) followed by Systemic Repeated Dose Toxicity and Reproductive Toxicity/Developmental Toxicity (seven members each).

5.4. Literature Survey Results: Evidence Maps of Exposure Data

The exposure evidence maps below describe high-level observations of the Level 2, 3, and 3B literature surveys in the indicated spreadsheet files.[26] Level 3B tagging was performed on a subset of toxicity exposure literature reviews selected from Level 3 to identify even more specific information for the chemicals in these references. The database counts indicate the number of entries in the Multimedia Monitoring Database (MMDB). The unit for PDF counts is

[26] Exposure evidence map files are available on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022.

the individual PDF file. PHBAF analogs were not included in the exposure evidence map analyses because exposure to the analogs is outside the scope of the current project.

The general observations from the Level 2, 3, and 3B reviews described below are that TBBPA was the most data rich PHBAF member in each category and had the most representation across exposure categories for database and PDF reviews. The second most data rich PHBAF member for exposure information was TBBPA-DBPE.

5.4.1. Summary of Level 2

The MMDB database and PDF searches identified exposure data sources for 12 of 14 PHBAF members.[27] The PHBAF members with the most data sources were TBBPA (131), TBBPA-DBPE (19), and TBBPA-BAE (11). Table 5-10 summarizes how many PHBAF members had different degrees of data source abundance. The PDFs provided most of the data sources and covered 12 PHBAF members; the database provided one exposure data source for TBBPA only.

Table 5-10. Distribution of Exposure Data Source Abundance Levels at Level 2

Distribution of Number of Data Sources Available for Each Chemical	Number of Chemicals with Level 2 Exposure Data Sources
	PHBAF Chemicals (n = 14)
21+	1
6–20	5
1–5	6
0	2

5.4.2. Summary of Levels 3 and 3B

The "EXP Integrated" tabs from each file contains Level 3 and 3B exposure data counts.[28] The Level 3 integrated counts indicate the number of data sources per chemical from the MMDB database and identified PDFs. Level 3 counts were classified into six exposure data type categories. Integrated Level 3B counts report the sum of data sources from MMDB and a sample of selected PDFs. At Level 3B, reviewers tagged the data sources to subcategories to provide additional details of specific data types. Table 5-11 summarizes how many PHBAF members had different degrees of Level 3 exposure data source abundance.

[27] Exposure evidence map files are available on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022.
[28] Exposure evidence map files are available on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022

Table 5-11. Distribution of Exposure Data Source Abundance Levels at Level 3

Distribution of Number of Data Sources Available for Each Chemical	Number of Chemicals with Level 3 Exposure Data Sources					
	PHBAF Chemicals (n = 14)					
	Environmental Monitoring	Biomonitoring/ Personal Monitoring	Source Characterization	Epidemiology – Population Group	Modeled Concentrations	Modeled Human Dose
21+	1	1	1	0	0	1
6–20	1	0	3	0	1	0
1–5	6	3	8	1	0	3
0	6	10	2	13	13	10

Environmental Monitoring data sources were available for eight PHBAF members at Level 3 review. Seven PHBAF members had data in the database and the selected PDFs at Level 3B review. This category was separated into six subcategories for Level 3B review: Indoor/Personal Air, Indoor Dust, Outdoor Air, Food/Dietary, Soil, and Drinking Water.

- PHBAF members TBBPA and TBBPA-DBPE each had data sources in all of the subcategories.
- PHBAF member TBBPA had the highest data source counts in each subcategory.
- The subcategory with data for the most PHBAF members (seven) was Drinking Water.

Biomonitoring/Personal Monitoring data sources were available for four PHBAF members at Level 3 review. Three PHBAF members had data in the database and the selected PDFs at Level 3B review. This category was separated into five subcategories for Level 3B review: Blood/Serum, Urine, Breast Milk/Lipids, Skin/Dermal, and Human (Other).

- PHBAF member TBBPA had data sources in all of the subcategories and had the highest data source counts in all categories except Urine.
- PHBAF member 2,2',6,6'-Tetrachlorobisphenol A had at least one data source in all subcategories except Skin/Dermal.

Source Characterization data sources were available for 12 PHBAF members at Level 3 review. Nine PHBAF members had data in the database and the selected PDFs at Level 3B review. This category was separated into four subcategories for Level 3B review: Product Testing: Content Only, Product Testing: Emission/Migration Data, Nonexperimental Product- or Chemical-Specific Modeling Inputs, and Other Qualitative or Quantitative Description of Product Use or Class/Chemical.

- PHBAF member TBBPA had data sources in all of the subcategories.
- PHBAF member TBBPA-BAE had data sources in all subcategories except Emission/Migration Data.

- PHBAF member 2,2',6,6'-Tetrachlorobisphenol A had at least one data source in all subcategories except Nonexperimental Product or Chemical-Specific Modeling Inputs.
- The subcategory with data for the most PHBAF members (nine) was Other Qualitative or Quantitative Description of Product Use or Class/Chemical.

Environmental Epidemiology[29] data sources were available for one PHBAF member (TBBPA) at Level 3 review. No data under this category were identified for any of the PHBAF members in the Level 3B review. The subcategories were Children; Adult, Non-Occupational; and Other, Specify (with Suggestions).

Modeled Concentrations data sources for one PHBAF member (TBBPA) were identified at Level 3 review. Level 3B reviews of the database and the selected PDFs found two sources in each of three subcategories (Indoor Concentration, Outdoor Concentration, and Dietary/Food) for TBBPA.

Modeled Human Dose data sources were available for four PHBAF members at Level 3 review. The same four PHBAF members had data in the database and the selected PDFs at Level 3B review. The subcategories were Children; Adult, Non-occupational; and Other, Specify (with Suggestions).

- TBBPA had eight and 10 data sources, respectively, for the subcategories Children and Adult, Non-occupational.
- The remaining three PHBAF members (TBBPA-DBPE, TBBPA-BAE, and TBBPA-BHEE) each had one data source in two subcategories, Children and Adult | Non-occupational.
- No PHBAF members had data identified as Other, Specify (with Suggestions).

5.5. Literature Survey Results: Summary of Existing Human Health Risk Assessments

None of the "Database" (DB) tabs at Levels 2, 3, or 3B reported risk assessment data sources. Therefore, the Integrated and PDF data counts for Human Health Risk Assessments are identical at all levels. In the files that reported PDF data sources, human health risk assessments were included in the tabs for spreadsheets displaying toxicity data sources.

5.5.1. Summary of Level 2

The "Integrated" tab contains summed Level 2 risk data counts from PDF sources.[30] No risk data were found in the databases. Four PHBAF members and no analogs had PDF data sources for risk at Level 2 review. Table 5-12 summarizes how many PHBAF members had different degrees of data source abundance at Level 2. TBBPA had 30 risk assessment PDFs. TBBPA-DBPE, TBBPA-BAE, and TBBPA-BHEE each had one risk assessment PDF at Level 2.

[29] The category *Environmental Epidemiology* here was identified as "*Epidemiology – POP Group*" in the "EXP_Integrated_C" tab of the Excel file, which can be found on the CPSC Organohalogen Flame Retardant Chemicals Assessment website). The change was made in this document for clarity.
[30] Risk evidence map files are available on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022

Table 5-12. Distribution of Human Health Risk Data Sources Abundance Levels at Level 2

Distribution of Number of Data Sources Available for Each Chemical	Number of Chemicals with Levels 2 and 3 Exposure Data Sources
	PHBAF Chemicals (n = 14)
21+	1
6–20	0
1–5	3
0	10

5.5.2. Summary of Levels 3 and 3B

The "Integrated" tab for the Level 3 file contains the *Human Health Risk Assessment* counts from PDF data sources.[31] The "TOX_PDF" tab for Level 3B contains the *Human Health Risk Assessment* counts from PDFs that were selected for 3B extraction. The counts indicate the number of PDFs identified per chemical for each Noncancer and Cancer risk assessment. The counts of PHBAF members at different degrees of abundance for human health risk were the same at Levels 2 and 3 (see Table 5-12).

Human Health Risk Assessment data were available for four PHBAF members and no analogs at Level 3 review. The same four PHBAF members had data in the selected PDFs at Level 3B review. The subcategories used in this category were Noncancer Risk and Cancer Risk. CPSC staff observed the following:

- PHBAF member TBBPA had seven Noncancer Risk and three Cancer Risk data sources.
- PHBAF members TBBPA-DBPE, TBBPA-BAE, and TBBPA-BHEE each had one data source for Noncancer Risk and none for Cancer Risk.

5.6. Literature Survey Results: Key References

Among the literature survey results are several references from authoritative sources. These references include a toxicological profile by the Agency for Toxic Substances and Disease Registry, technical reports from the National Toxicology Program, EPA assessments and evaluations, Health Canada assessments, European Union risk assessment reports, International Agency for Research on Cancer evaluations, and Organisation for Economic Co-operation and Development assessments. Each of these references addressed one or more PHBAFs. TBBPA was the subject of several of these reports. TBBPA and three other PHBAFs (TBBPA-BDBPE, TBBPA-BAE, TBBPA-BHEE) were included in multiple reports . One report (Danish EPA) included five additional subclass chemicals. The four chemicals (TBBPA, TBBPA-BDBPE, TBBPA-BAE, TBBPA-BHEE) included in multiple references are also among the PHBAFs most frequently cited in the Market and Use Report and literature survey. These reports suggest the existence of data about these chemicals, including hazard and potential

[31] Risk evidence map files are available on the CPSC Organohalogen Flame Retardant Chemicals Assessment website or Docket No. CPSC-2015-0022.

exposures, and may be useful references for CPSC staff evaluations of these and other PHBAFs.

6. Scoping Determination and Next Steps

6.1. Scoping Determination

Informed by initial review of the market and use research, evidence maps, and availability of physicochemical data for the PHBAF subclass and its analogs, and the criteria described in Section 4.1, Criteria for Scoping Determination, CPSC staff concludes, at the time of writing, that **the PHBAF subclass has sufficient data to proceed with risk assessment**.

The criteria for sufficiency for hazard assessment for the subclass require that the subclass and analogs must have at least one data rich chemical, multiple chemicals with some data, and a minority of chemicals that are "no data" substances.

CPSC staff concludes that the subclass includes up to four data rich PHBAF chemicals and that a majority of PHBAF chemicals and some analogs have some data. The evidence maps show that many PHBAF chemicals have data in the Animal Toxicity or Accepted Alternative category, including among acute, systemic or repeated dose toxicity, or reproductive/developmental studies. In addition, a majority of PHBAF chemicals and some analogs have data in the experimental, mechanistic, and QSAR categories, all of which may be used to support further analyses, including performing read-across analyses for predictions among class members with less available data.

The criteria for sufficiency for exposure assessment for the subclass require that the subclass must have at least one data rich chemical and multiple chemicals with some data.

CPSC staff concludes that the subclass includes up to four data rich PHBAF chemicals and the evidence maps show that a majority of PHBAF chemicals have some exposure data. In addition, according to available data sources, all 14 PHBAF chemicals have some use information from the market-use report.

Following the determination that the PHBAF subclass has sufficient data to proceed with risk assessment, the sections below outline the next steps that CPSC staff plans to take, resources permitting. Below, CPSC staff provides plans for analysis to complete a class-based risk assessment. The first analysis plan describes how CPSC staff will consider data in the development of a class-based hazard identification and dose-response assessment for select endpoints. The second analysis plan describes how CPSC staff will consider data in a class-based human exposure assessment. The last step of both analysis plans is identical in that CPSC staff will consider how to combine class-based human exposure estimates with class-based toxicity reference values in a class-based risk assessment.

6.2. Next Steps for Class-Based Hazard Assessment

6.2.1. Analysis Plan

CPSC staff plans to actively work on the remaining list of activities outlined below. Many of these activities can be undertaken concurrently, as resources are available. Before completing a hazard analysis, CPSC staff expects to consider and analyze data that could inform hazard identification and dose-response as follows if resources are available:

1. CPSC staff, in coordination with the Division of Translational Toxicology (DTT) at the National Institute of Environmental Health Sciences, is working on a comprehensive literature search. Available toxicity information from PHBAF class members and analogs will be further summarized and integrated after this search is complete. After the search, staff will refine the list of data rich PHBAFs, data rich PHBAF analogs, PHBAFs with some toxicity information, and PHBAFs with no toxicity information.
2. CPSC staff plans to complete a systematic evidence map that will be based on a scoping review in coordination with DTT. This evidence map will include a wide range of toxicity data (e.g., animal, human, mechanistic, QSAR, read-across, new approach methodologies [NAMs][32]) from the comprehensive literature search.
3. CPSC staff will refine the NAS analog list and characterize analog substances for the PHBAF class that are both chemically and toxicologically similar and have any amount of empirical toxicity information. Analog substances that are both data poor and not sufficiently similar to PHBAF class members will be deprioritized. CPSC staff's initial survey shows that empirical toxicity data are available for two analogs and empirical toxicokinetic data are available for six analogs.
4. CPSC staff will estimate major metabolites of PHBAF class members by interpreting results from the major metabolite prediction tools, such as GLORYx and the OECD QSAR toolbox, and comparing these results with data presented in the literature. CPSC staff will consider predicted and measured metabolites to inform class-based approaches for hazard identification.
5. CPSC staff plans to use a read-across approach that incorporates multiple types of data (i.e., animal, human, mechanistic, QSAR, read-across). Data rich PHBAF class members and analogs with available toxicity data can be used to read-across to PHBAF class members with insufficient data to estimate toxicity reference values for one or more endpoints of concern. The initial CPSC literature survey suggests that toxicity endpoints that are likely higher priority for the PHBAF class are carcinogenicity, systemic repeated-dose toxicity, mutagenicity, genotoxicity, reproductive toxicity, developmental toxicity, developmental neurotoxicity, and endocrine disruption. Toxicity endpoints that are likely lower priority for the PHBAF class are acute toxicity, irritation, and sensitization.

[32] NAMs include any technology, methodology, approach, or combination thereof that can be used to provide information on chemical hazard and risk assessment that avoids the use of intact animals. NAM studies may include studies using human or animal cells and tissues (i.e., in vitro assays, ex vivo studies), toxicity testing using alternative animal species, such as zebrafish and nematodes, and a variety of computational modeling approaches.

6. CPSC staff will identify a smaller number of endpoint(s) and studies that are candidates for identifying points of departure (POD) and generating toxicity reference values for multiple PHBAF class members. PODs may be developed using a wide range of toxicity studies (e.g., animal, human, NAM, QSAR, read-across). CPSC staff will identify studies with a range of reported doses and associated contextual information when developing dose-response information. Benchmark dose modeling will be used as appropriate.
7. CPSC staff will compare these values with toxicity reference values developed by other organizations for PHBAF class members.
8. CPSC staff will explore the variability and uncertainty associated with dose response values for PHBAF chemicals within the class.
9. CPSC staff will use information developed in a class-based hazard assessment and dose-response assessment to support a class-based risk assessment for PHBAFs.

6.2.2. Initial Human Health Hazard Observations for Class-Based Assessment of PHBAFs

The primary objective of completing a literature survey for a subclass of OFRs is to array available information and determine whether a class-based assessment is possible. CPSC staff considers class-based exposure assessment possible for any class if data on consumer uses and physicochemical properties are available. However, CPSC staff considers class-based hazard assessment as highly data dependent. Thus, whether a class-based risk assessment is possible depends on the availability of different types of human hazard data. When sufficient human health hazard data were identified from the literature survey, this section of the scope document includes initial observations informed by review of select data sources.

NASEM included PHBAFs as one of two case studies in its 2019 report. NASEM focused on the effects on thyroid hormones and developmental effects on morphology and behavior but also summarized the data on genotoxicity, repeated dose toxicity, and carcinogenicity.

NASEM (2019) noted that TBBPA decreased serum thyroxine (T4) concentrations in subchronic studies in rats, with no effect on either triiodothyronine (T3) or thyroid-stimulating hormone (TSH) concentrations. Health Canada (2013) did not consider this change to be adverse, in the absence of other relevant thyroid-related effects, given that the active form (T3) was not affected. NASEM (2019) described the thyroid hormone data as discordant between rodents and zebrafish and noted a zebrafish study that observed increased T4 and decreased T3, and another that reported “interference with thyroid hormone homeostasis.” Upregulation of clearance enzymes and increased hepatic and uterine expression of the gene that encodes thyroid receptor TRα have been reported in rats and may provide the mechanism for effects on thyroid hormone homeostasis (NASEM, 2019).

NASEM (2019) concluded, based on the available rodent data, that the PHBAF subclass has “minimal developmental effects in mammals.” TBBPA and TBBPA bis(2-hydroxyethyl) ether had positive or mixed results for teratogenesis and locomotor activity in zebrafish, whereas TBBPA bis(2,3-dibromopropyl) ether and TBBPA-BGE were negative in zebrafish.

Other toxicity data are available primarily for TBBPA. A systematic review and meta-analysis of rodent studies on TBBPA found a statistically significant effect on the male reproductive system,

specifically on sperm quality, hormone levels, and gene expression, even though the effect in most individual studies was not statistically significant (Wu et al., 2021). In a weight of evidence evaluation, the European Union (EU RAR, 2006, as cited by Health Canada, 2013) concluded that TBBPA had no significant estrogenic potential, based on the evidence from in vitro screening assays.

Health Canada (2013) based its exposure limit for TBBPA on enlargement and very slight focal necrosis of hepatocytes in female offspring of mice exposed via diet from the first day of gestation through weaning. EPA (2015) considered slight kidney lesions in newborn rats treated with TBBPA on postnatal days 4–21 to be the critical noncancer effect, also noting the potential for cancer. The kidney lesions were not observed in 5-week-old rats receiving higher doses for 18 days, and so the effects in neonatal rats were attributed to immature metabolic capability and/or immature kidneys. NASEM (2019) reported that there were no adverse effects in repeated dose studies of TBBPA bis(2,3-dibromopropyl ether) in rats and mice (subchronic) and TBBPA bis(2-hydroxyethyl) ether (28-day, species not reported). Increased serum enzymes indicative of liver toxicity and increased liver weight were the critical effects in a 28-day study of TBBPA-BGE in rats.

There is general agreement that PHBAFs as a subclass are negative for gene mutation in bacteria and lack structural alerts suggesting a mutagenic potential (NASEM, 2019; Health Canada, 2013, US EPA, 2015).

NTP (2014) concluded there was clear evidence of carcinogenic activity of TBBPA in female Wistar Han rats based on increased incidences of uterine epithelial tumors. NTP concluded there was some evidence of carcinogenic activity of TBBPA in male B6C3F1/N mice based on the increased incidences of hepatoblastoma, but EPA (2015) did not consider these tumors related to TBBPA. However, EPA (2015) considered TBBPA to be associated with hemangiomas and hemangiosarcomas in male mice and also noted hemangiosarcomas in male rats. NTP concluded there was equivocal evidence of carcinogenic activity of TBBPA in male Wistar Han rats and no evidence of carcinogenic activity of TBBPA in female B6C3F1/N mice. EPA (2015) classified TBBPA as likely to be carcinogenic to humans, based on uterine epithelial tumors in female rats and hemangiomas and hemangiosarcomas in male mice.

EPA (2015) noted a number of potential MOAs for the uterine tumors, with perhaps the most support for increased estrogen due to competitions for transferases but noted that the data are not adequate to conduct a rigorous MOA evaluation. MOA was not discussed for other tumor types.

NASEM (2019) noted that some subclass members may be expected to exhibit differences in toxicity compared to TBBPA for several reasons. TBBPA and TCBPA have phenolic carbons that lead to (or are predicted to lead to) conjugation with glucuronic acid or sulfate, and therefore rapid excretion. Differences in R group substitutions on the phenolic carbons may lead to altered metabolism and slower excretion. Differences in molecular weight and water solubility can also lead to differences in toxicity. For example, EPA (2015) stated that low absorption and associated low toxicity were either observed (TBBPA bis(2,3-dibromopropyl ether) or expected (TBBPA diallyl ether), despite potential as alkylating agents. In contrast, TBBPA dimethyl ether

differs from TBBPA only in the substitution of a phenolic hydrogen with a methyl group, and so EPA (2015) suggested that read-across from TBBPA would be possible.

6.3. Next Steps for Class-Based Exposure Assessment

6.3.1. Analysis Plan

CPSC staff plans to actively work on the remaining list of activities outlined below. Many of these activities can be undertaken concurrently, as resources are available. Before completing a hazard analysis, CPSC staff expects to consider and analyze data that could inform hazard identification and dose-response as follows, as resources permit:

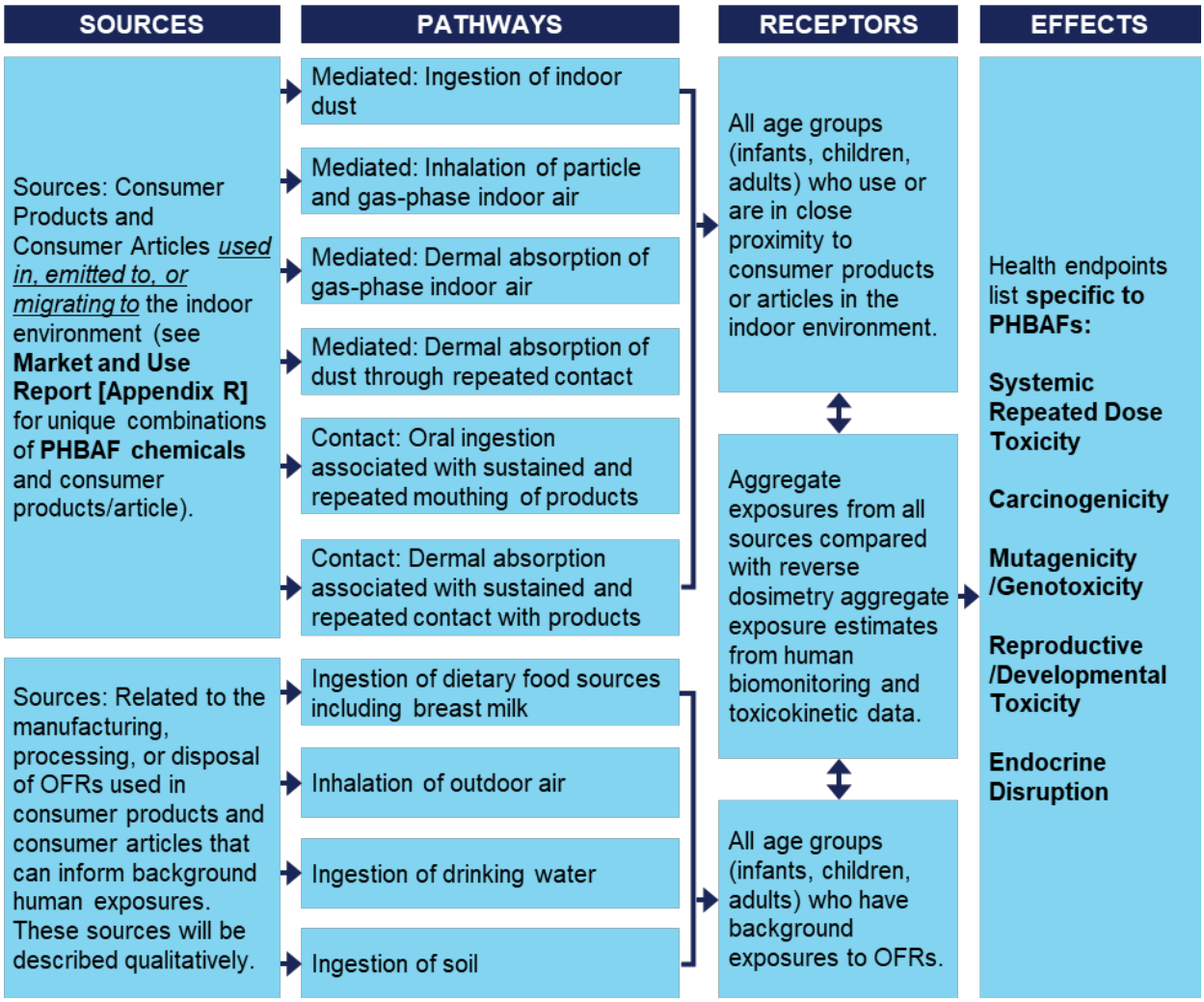
1. CPSC staff, in coordination with DTT staff, is working on a comprehensive literature search. Available exposure information from PHBAF class members will be further summarized and integrated after this search is complete. After the search, staff will refine the list of data rich PHBAFs, PHBAFs with some exposure and use information, and PHBAFs with no exposure and use information.
2. Using the market and use research, CPSC staff expects to compile a list of PHBAF chemicals that have been or could be used in consumer products. While 14 chemicals had some market-use information, four PHBAF chemicals had more market and use information that could be used to inform analyses for PHBAF chemicals with less information. CPSC staff will characterize uses for PHBAFs according to available information and consider temporal trends when developing exposure scenarios.
3. CPSC staff will characterize the uses identified in the market and use research and combine this information with likely exposure pathways and populations exposed to define unique combinations of exposure scenarios for chemical substances within the class. Depending on available information, CPSC may be able to quantify exposure scenarios for between eight and 14 PHBAF subclass members.
4. Exposure pathways with likely higher potential for PHBAF class members include dietary ingestion, contact exposures with consumer products and articles, indoor dust ingestion, and inhalation of indoor air. Exposure pathways with likely lower potential for PHBAF class members include inhalation of ambient air, drinking water ingestion, and soil ingestion. CPSC staff will review available environmental monitoring data to determine a range of potential concentrations to which people could be exposed. There are 12 chemicals in the class with source characterization data, eight chemicals in the class with environmental monitoring data, and eight chemicals in the class with both types of data.
5. CPSC staff plans to review measurement techniques and analytical methods and assess how they have changed over time with regard to identification and quantification of PHBAF chemicals. Lack of detection in older studies may be due to older analytical methods with higher detection limits, whereas presence in newer studies may be due to newer analytical methods with lower detection limits. CPSC staff plans to evaluate reported methods and how they influence likely distributions of OFRs in different environmental media or biological matrices.

6. CPSC staff will explore the connection between consumer product sources and reported levels in environmental media by estimating environmental concentrations for a range of uses and determining whether these estimates fall within the range of reported environmental monitoring data. CPSC staff plans to consider indoor exposure modeling, modeling approaches specific to semi-volatile organic compounds (SVOCs), and product-testing measurement techniques that characterize emissions or migration of OFRs from products into the indoor environment. When environmental monitoring is not available for comparison, CPSC staff will estimate environmental concentrations for the range of reported uses. There are four chemicals in the class with source characterization data and no corresponding environmental monitoring data.
7. CPSC staff will explore the connection between reported or estimated environmental concentrations and reported exposures from human biomonitoring data. First, doses will be estimated using reported or estimated environmental concentrations and population-specific exposure factors and activity patterns. Second, doses will be estimated using reported human biomonitoring data and reported or estimated toxicokinetic data. There are four PHBAF class members with both environmental monitoring data and human biomonitoring data.
8. CPSC staff plans to use multiple approaches to estimate exposures and doses for multiple age groups and populations. CPSC staff plans to develop both deterministic and probabilistic estimates of dose, as data allow. CPSC staff will explore the variability and uncertainty associated with exposure and dose estimates for the population groups included in the human exposure assessment.
9. CPSC staff will use information developed in a class-based exposure assessment to support a class-based risk assessment for PHBAFs.

6.3.2. Conceptual Exposure Model

A conceptual exposure model visually represents connections between sources, pathways, receptors, and health effects. Figure 6-1 shows the conceptual exposure model for the PHBAF subclass. Sources are grouped into (i) those that can be related back to consumer products and (ii) all other sources that can inform background exposures. These sources will be part of a generic background exposure scenario. Each product/source will be part of an exposure scenario and quantified. Exposure pathways similarly are grouped into pathways related to emission or migration from consumer products and pathways related to occurrence in nonconsumer product-related media. Receptors include human populations of all age groups for which human biomonitoring data will be used to inform ranges of aggregate exposures from all sources. Finally, human health effects most likely to be considered for PHBAFs are listed.

Figure 6-1. PHBAF Conceptual Exposure Model



7. References

Bevington, C., Williams, A.J., Guider, C., Baker, N.C., Meyer, B., Babich, M.A., Robinson, S., Jones, A., Phillips, K.A. (2022). Development of a Flame Retardant and an Organohalogen Flame Retardant Chemical Inventory. Sci Data 9, 295. https://doi.org/10.1038/s41597-022-01351-0.

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European Union Risk Assessment Report (EU RAR). (2006). *EU RAR CAS No. 79-94-7 EINECS: 201-236- 9 2,2',6,6'-tetrabromo-4,4'-isopropylidenediphenol (tetrabromobisphenol A or TBBPA) Part II human health*. European Commission Joint Research Centre, EUR 22161 EN 4th Priority List Volume:63. Available from: http://europa.eu.int. As cited by Health Canada, 2013.

Health Canada. (2013). *Screening assessment report: Phenol, 4,4'-(1-methylethylidene) bis[2,6-dibromo- Chemical Abstracts Service Registry Number 79-94-7; ethanol, 2,2'-[(1-methylethylidene)bis[(2,6-dibromo-4,1-phenylene)oxy]]bis Chemical Abstracts Service Registry Number 4162-45-2, benzene; 1,1'-(1-methylethylidene)bis[3,5-dibromo-4-(2-propenyloxy)- Chemical Abstracts Service Registry Number 25327-89-3*. https://www.ec.gc.ca/ese-ees/default.asp?lang=En&n=BEE093E4-1

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National Toxicology Program (NTP). (2014). *NTP technical report on the toxicology studies of tetrabromobisphenol A (CAS No. 79-94-7) in F344/NTac rats and B6C3F1/N mice and toxicology and carcinogenesis studies of tetrabromobisphenol A in Wistar Han [Crl:WI(Han)] rats and B6C3F1/N mice (gavage studies)* (NTP TR 587). U.S. Department of Health and Human Services, Public Health Service. https://doi.org/10.22427/NTP-TR-587

United States Environmental Protection Agency (US EPA). (2015). *TSCA work plan chemical problem formulation and initial assessment: Tetrabromobisphenol A and related chemicals cluster flame retardants* (EPA Document No. 740-R1-4004). Office of Chemical Safety and Pollution Prevention. https://nepis.epa.gov/Exe/ZyPURL.cgi?Dockey=P100N2CG.txt

Wu, H., Wang, J., Xiang, Y., Li, L., Qie, H., Ren, M., Lin, A., & Qi, F. 2021. Effects of tetrabromobisphenol A (TBBPA) on the reproductive health of male rodents: A systematic review and meta-analysis. *Science of the Total Environment*, *781*, Article 146745. https://doi.org/10.1016/j.scitotenv.2021.146745

8. Appendix: Supporting Files

The following supporting files are available on the CPSC Organohalogen Flame Retardant Chemicals Assessment website. They can also be found on Docket No. CPSC-2015-0022.

Guide: CPSC staff's approach for conducting Literature Surveys

University of Cincinnati (UC). (2022). *Literature survey guide: Draft 6* [Literature Survey Guide Draft 6_10.17.22_final.docx]. U.S. Consumer Product Safety Commission.

Market and Use Profile Volume 1 and 2

Industrial Economics Incorporated (IEc). (2022). *Characterizing organohalogen flame retardant (OFR) chemistries, sources, and uses in United States and international markets: Vol. 1 – Main report* [Vol 1 Main Report 03.24.2022_Final.pdf]. U.S. Consumer Product Safety Commission.

Industrial Economics Incorporated (IEc). (2022). *Characterizing organohalogen flame retardant (OFR) chemistries, sources, and uses in United States and international markets: Vol. 2 – Appendices* [Vol 2 Appendices 03.09.2022_Final.pdf]. U.S. Consumer Product Safety Commission.

Chemical Descriptors and Physicochemical Properties for PHBAF Class and Analogs

University of Cincinnati (UC). (2022). *PHBAF chemical descriptors and physicochemical properties* [PHBAF Chemical Descriptors and Physicochemical Properties.xlsx]. U.S. Consumer Product Safety Commission.

Literature Survey Results

University of Cincinnati (UC). (2022). *PHBAF level 2 evidence maps* [PHBAF Level 2 Evidence Maps 12.2.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHBAF level 3 evidence maps* [PHBAF Level 3 Evidence Maps 12.2.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHBAF level 3B evidence maps* [PHBAF Level 3B Evidence Maps 12.2.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHBAF PDF 3B extraction final* [PHBAF PDF 3B Extraction Final 2.28.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHBAF tox individual database evidence maps - levels 2, 3, 3B* [PHBAF Tox Individual Database Evidence Maps - Levels 2, 3, 3B - 12.2.22.xlsx]. U.S. Consumer Product Safety Commission.

Market and Use Profile Supporting Files

Industrial Economics Incorporated (IEc). (2022). *Characterizing organohalogen flame retardant (OFR) chemistries, sources, and uses in United States and international markets: Attachment A: Standard operating procedure for producing data source outputs* [Attachment A_Data SOP.pdf]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research CompTox chemical information* [OFR_universe_wCompTox_batch_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research CompTox chemical synonyms* [OFR_universe_wCompTox_syns_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research CompTox experimental data* [OFR_universe_wCompTox_exp_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research CompTox predicted data* [OFR_universe_wCompTox_pred_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research CompTox product use* [OFR_universe_wCompTox_prod_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research data synthesis* [Data Source Synthesis_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research database readme* [00_ReadMe_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research ECHA plastics* [OFR_universe_wECHA_add_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research ECHA sources* [OFR_universe_wECHA_links_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research EPA TRI* [OFR_universe_wTRI_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research field counts* [04_FieldCounts_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research fields list* [03_FieldsList_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research NORMAN database* [OFR_universe_wNorman_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research OFR chemical list* [01_Attachment 1_OFR_universe_cid_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research PubChem chemical data* [OFR_universe_wPCPy_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research PubChem chemical identification* [OFR_universe_wPCBrowser_ID_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research PubChem mass spec* [OFR_universe_wPCBrowser_MS_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research PubChem MassBank spectra* [OFR_universe_wPCBrowser_MoNA_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research PubChem NORMAN* [OFR_universe_wPCBrowser_Norman_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research QSUR* [OFR_universe_wQSUR_03042022.xlsx]. U.S. Consumer Product Safety Commission.

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