United States
Consumer Product Safety Commission

Organohalogen Flame Retardant Scope Document: Polyhalogenated Aliphatic Chain Subclass

February 2024

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.

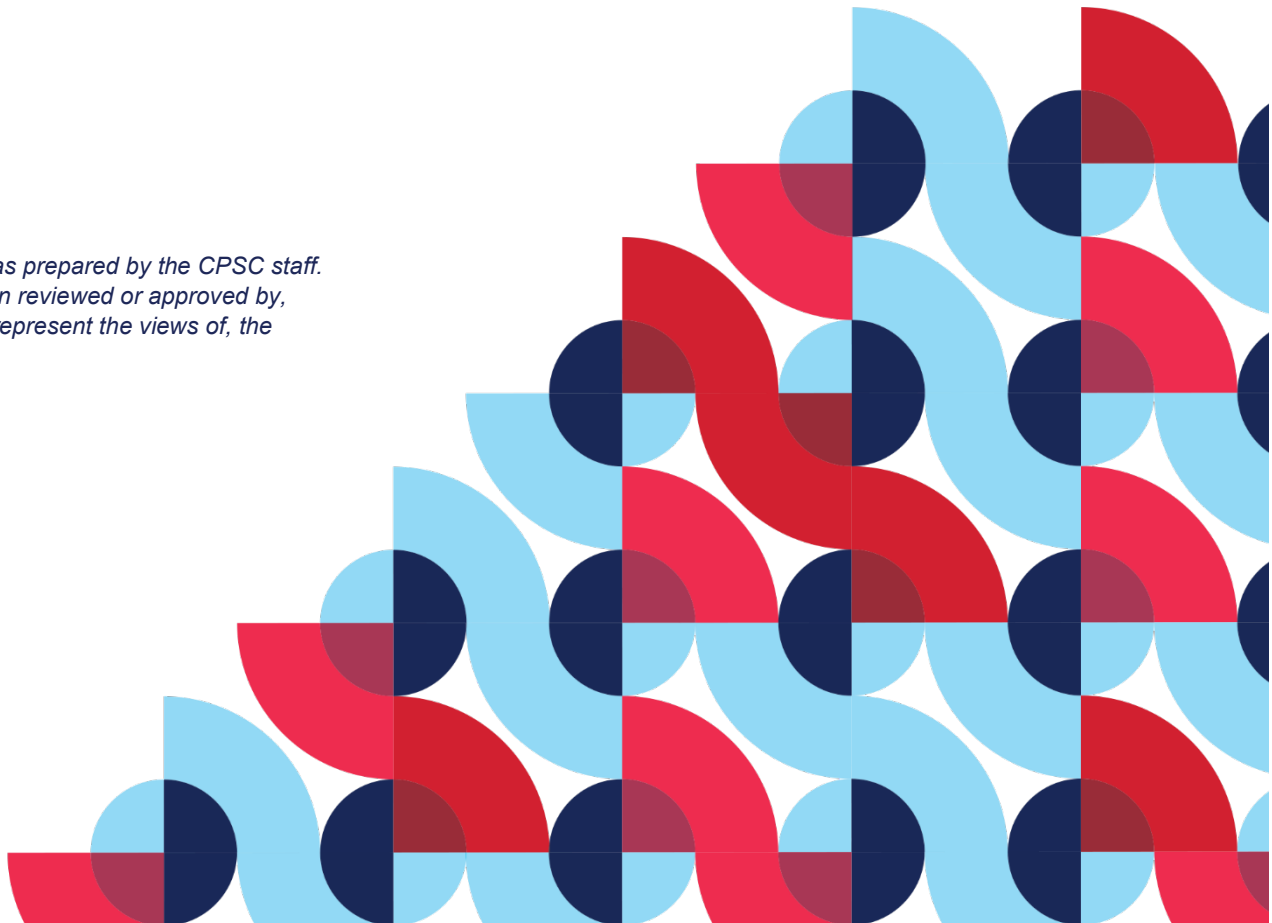


Table of Contents

1. Executive Summary

This scope document addresses the polyhalogenated aliphatic chains (PHACh) 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 period of time.

Informed by initial review of the market and use research, evidence maps, and availability of physicochemical data for the PHACh 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 PHACh 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 PHACh 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]

[1] Project documents, including CPSC staff reports, contractor reports, and key references may be found on the CPSC Organohalogen Flame Retardant Chemicals Assessment website

- 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. A key conclusion of the Committee is that OFRs cannot be treated as a single class. Rather, the Committee identified 14 subclasses of OFRs, based on chemical structure, physicochemical properties of the chemicals, and predicted biological activity.

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.

(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 would occur prior to finalizing any subclass risk assessment if carcinogenicity, mutagenicity, or reproductive/developmental toxicity were chosen as relevant endpoints.

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 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 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,

[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.

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 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.[10] 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

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

[10] Active chemicals are those that have been reported to EPA for manufacture or processing in the U.S., including those reported within a 10-year time period ending on June 21, 2016. Inactive chemicals are those that have not been reported and are, therefore, not considered to be in commercial use.

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 their 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

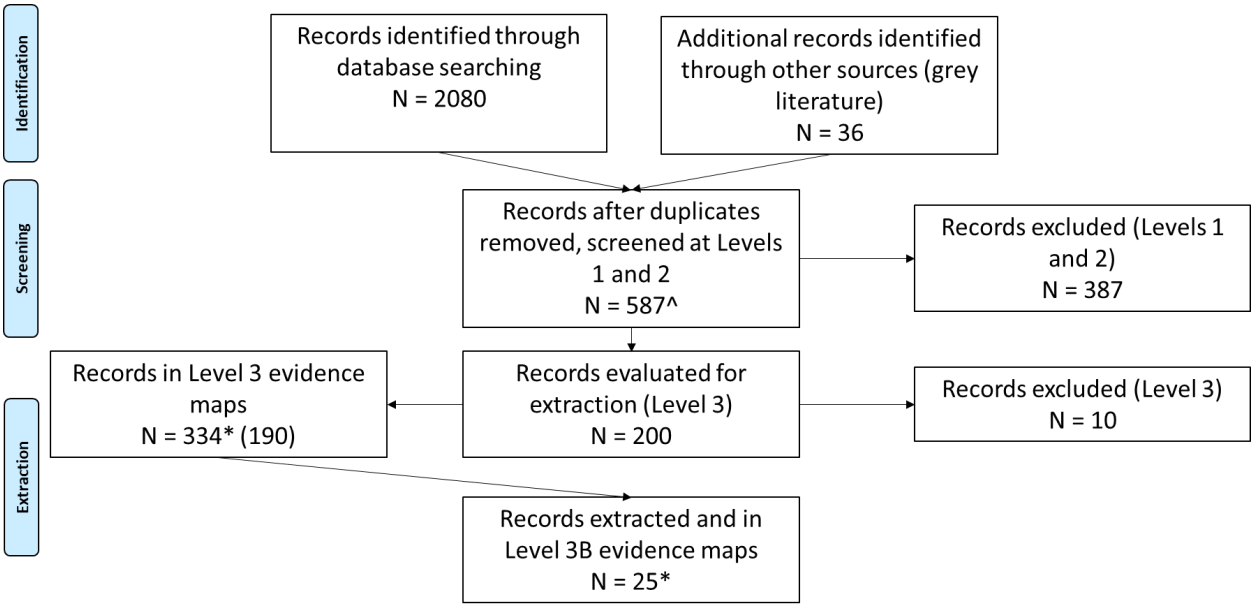
The OFR literature survey was intended to gather readily available toxicity, exposure, and risk information to characterize the types and amounts of data available for chemicals (and analogs) within a class. CPSC staff defined data sources for the literature survey effort as toxicity, exposure, and chemistry 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.[11] **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.

[11] 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 subclass, and between this subclass and previous subclasses.
*PHACh evidence maps contain additional references uploaded with other subclasses. Number in parentheses is the number of references identified by searching for the PHACh subclass only, excluding the references identified by searching for other subclasses.

5. Scoping for PHAChs

5.1. PHACh Subclass Chemistry

The PHACh subclass generally consists of chemicals containing straight or branched chains of carbons with halogenated substituents on the chain. In particular, members of this subclass all have a carbon-halogen chemical bond. The different carbon chain lengths, saturation (double vs single carbon-carbon bonds) and presence of alcohol (-OH) functional groups on certain chains may lead to chemistry-based differences throughout this subclass despite structural similarities amongst the members.

Table 5-1 lists 47 individual chemicals in the PHACh subclass.

Table 5-1. List of Chemicals in PHACh Subclass

	CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
1	106232-85-3	Alkanes, C18-20, chloro	NA	NA
2	106232-86-4	Alkanes, C22-40, chloro	NA	NA
3	108171-26-2	C10-12 chloroalkanes / 2,3,4,6,7,8-hexachlorodecane	NA	CCC(C(C(CC(C(C(C)Cl)Cl)Cl)Cl)Cl)Cl)Cl

	CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
4	108171-27-3	Chloro C22-26 alkanes / 1,3,7,11,15,19,23-Heptachlorotetracosane	NA	CC(CCCC(CCCC(CCCC(CCCC(CCCC(CCCl)Cl)Cl)Cl)Cl)Cl)Cl
5	109678-33-3*	1-Propanol, 3,3'-oxybis[2,2-bis(bromomethyl)-	NA	C(C(COCC(CO)(CBr)CBr)(CBr)CBr)O
6	125512-87-0	Hexabromohexane	NA	NA
7	1372804-76-6	Alkanes, C14-16, chloro	NA	NA
8	1401974-24-0	Alkanes, C22-30-branched and linear, chloro	NA	NA
9	1402738-52-6	Alkanes, C24-28, chloro	NA	NA
10	1417900-96-9	Alkanes, C21-34-branched and linear, chloro	NA	NA
11	1522-92-5*	3-Bromo-2,2-bis(bromomethyl)propanol	BRN 1738921	C(C(CBr)(CBr)CBr)O
12	1852481-27-6*	2,3,4,5,6,8-Hexachlorodecane	Chlorowax 500C	CCC(CC(C(C(C(C(C)Cl)Cl)Cl)Cl)Cl)Cl
13	2097144-43-7	Alkanes, C20-28, chloro	NA	NA
14	2097144-45-9	Alkanes, C20-24, chloro	NA	NA
15	2097144-46-0	Hexacosane, chloro derivs.	BRN 1304582	NA
16	2097144-47-1	Octacosane, chloro derivs.	NA	NA
17	2097144-48-2	Octadecane, chloro derivs.	NA	NA
18	24173-07-7*	1,2,3,4-Tetrabromo-2,3-dimethylbutane	NA	CC(CBr)(C(C)(CBr)Br)Br
19	288260-42-4	Alkanes, C22-30, chloro	NA	NA
20	3234-02-4*	2,3-Dibromo-2-butene-1,4-diol	NA	C(C(=C(CO)Br)Br)O
21	3296-90-0*	Pentaerythritol dibromide	DBNPG	C(C(CO)(CBr)CBr)O
22	36483-57-5	Tribromoneopentyl alcohol	BRN 1738921; TBNPA	CC(C)(CBr)C(O)(Br)Br
23	36678-45-2*	2-Butene, 1,1,2,3,4,4-hexabromo-	NA	C(C(=C(C(Br)Br)Br)Br)(Br)Br
24	61788-76-9	Chloroalkanes	NA	CCCC(CCC(CC(C(CCC(CCC(C(CC(C)Cl)Cl)Cl)Cl)Cl)Cl)Cl)Cl
25	63449-39-8	Chlorinated paraffins	CP (mixed); SCCP; MCCP; LCCP;	CCCC(CCCC(CCC(CCC(CCC(CCCC(CCC)Cl)Cl)Cl)Cl)Cl)Cl
26	68527-01-5	Bromo chloro C12-30 a-alkenes	NA	CCCC(C(CCCCCC=C)Br)Cl
27	68527-02-6	Alkenes, C12-24, chloro	BRN 1737429	C=CCCCC=CCCCCCCl
28	68920-70-7	Alkanes, C6-18, chloro	NA	NA
29	68955-41-9*	1-Bromo-4-chlorodecane	NA	CCCCCCC(CCCBr)Cl
30	71011-12-6	Alkanes, C12-13, chloro	NA	NA

	CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
31	75-95-6*	Pentabromoethane	NA	C(C(Br)(Br)Br)(Br)Br
32	79-27-6*	1,1,2,2-Tetrabromoethane	BRN 1098321; Acetylene tetrabomide; Muthmann's liquid	C(C(Br)Br)(Br)Br
33	84082-38-2	C10-21, chloro	NA	NA
34	84776-06-7	Alkanes, C10-32, chloro	NA	NA
35	84776-07-8	Alkanes, C16-27, chloro	NA	NA
36	85049-26-9	Alkanes, C16-35, chloro	NA	NA
37	85422-92-0	Chlorinated paraffin oils	NA	NA
38	85535-84-8	C10-13 chloro alkanes	NA	NA
39	85535-85-9	Cercelor S 52 (MCCP)	NA	CC(CC(CC(CCCC(CC(CC(C)Cl)Cl)Cl)Cl)Cl)Cl)Cl
40	85535-86-0	C18-28 Chloroalkanes	NA	NA
41	85536-22-7	Alkanes, C12-14, chloro	NA	NA
42	85681-73-8	Chloroalkanes, C10-14	NA	NA
43	96-13-9*	2,3-Dibromopropanol	BRN 1719127; Brominex 257	C(C(CBr)Br)O
44	97553-43-0	Paraffins (petroleum), normal C>10, chloro	NA	NA
45	97659-46-6	Alkanes, C10-26, chloro	NA	NA
46	NO CAS RN	Long-chain chlorinated paraffins (C18-20)	LCCP	NA
47	NO CAS RN	Medium-chain chlorinated paraffins (C14-17)	MCCP	NA

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

Both the inventory and market-use report identify 47 chemicals for the PHACh subclass. This subclass contains many chemicals that are mixtures or otherwise are not classified as a TSCA Class one substance, which are substances with definite known structures. The evidence map did not include many of these non-discrete structures. The number of chemical substances included in the evidence maps is 21 of 47 chemicals listed in Table 5-1.

5.1.1. Physicochemical Property Summaries

The information collected to date led CPSC staff to find that experimental and predicted physicochemical data on PHACh chemicals are limited. Two PHACh subclass members have experimental data and 10 PHACh members have predicted data. Well-studied chemicals in this subclass include Pentaerythritol dibromide (DBNP, CAS RN 3296-90-0) and 1,1,2,2-Tetrabromoethane (CAS RN 79-27-6). From this data set, studied PHAChs have predicted boiling points ranging from 183°C to 426 °C, and vapor pressures from $1.58E^{-7}$ to $5.15E^{-1}$ mm Hg. Data show predicted water solubility values ranging from $5.49E^{-6}$ to $1.14E^{-1}$ mol/L. The octanol/water partition coefficient (K_{ow}) values, which are commonly expressed as log K_{ow}, range from 0.795 to 5.85.

5.2. Market and Use Summary for PHAChs

The OFR Market and Use Report, completed in March 2022, includes 47 PHACh chemicals.

- Forty-two PHACh chemicals had market and use information and five chemicals had no market and use information.
- According to EPA data, 21 PHACh chemicals were identified to be on the EPA TSCA chemical substance (active) inventory, three PHACh chemicals were identified on the TSCA (inactive) inventory, seven were on the CDR, and two were on the TRI program list.
- Two PHACh chemicals were identified in the Interstate Chemicals Clearinghouse (IC2) HPCDS.
- Twenty-one PHACh chemicals were identified in the targeted literature search.
- Fourteen PHACh chemicals had patent data.

5.2.1. PHAChs 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 42 PHAChs that are known to be or have been used in commerce, according to data available from these sources.

The five PHACh chemicals that are not known to be used in commerce are:

- Alkanes, C22-40, chloro (CAS RN 106232-86-4)
- Hexabromohexane (CAS RN 125512-87-0)
- Alkanes, C16-27, chloro (CAS RN 84776-07-8)
- Long-chain chlorinated paraffins (C18-20) (CAS RN NOCAS_872-42-2)
- Medium-chain chlorinated paraffins (C14-17) (CAS RN NOCAS_872-42-3)

Among the 42 PHACh chemicals used in commerce, 24 can be found in the TSCA inventory. Twenty-one chemicals are in the TSCA active inventory and three PHAChs are in the TSCA inactive inventory. In Table 5-2, PHACh chemicals found in 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).[12] Twenty-seven PHACh chemicals appear in one or more of these international inventories. In Table 5-2, the number of international registries for the identified PHAChs chemicals is listed in the ”International Inventories“ column.

[12] 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.

Twenty-one PHACh chemicals were identified in the literature through a targeted literature search.[13] 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.

Fourteen PHACh 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. For those chemicals that were not associated with a CID, "No CID" is reported in the Patents column.

Table 5-2. PHACh Chemicals Used in Commerce

CAS RN	Chemical Name	TSCA	International Inventories	Literature Cites	Patents
106232-85-3	Alkanes, C18-20, chloro	Active	2	1	No CID
108171-26-2	C10-12 chloroalkanes	Not found	1	2	0
108171-27-3	Chloro C22-26 alkanes	Not found	1	1	0
109678-33-3	1-Propanol, 3,3'-oxybis[2,2-bis(bromomethyl)-	Not found	1	0	16
1372804-76-6	Alkanes, C14-16, chloro	Active	0	0	No CID
1401974-24-0	Alkanes, C22-30-branched and linear, chloro	Active	0	0	No CID
1402738-52-6	Alkanes, C24-28, chloro	Active	0	0	No CID
1417900-96-9	Alkanes, C21-34-branched and linear, chloro	Active	0	0	No CID
1522-92-5	3-Bromo-2,2-bis(bromomethyl)propanol	Not found	2	2	2,244
1852481-27-6	2,3,4,5,6,8-Hexachlorodecane	Not found	Not found	0	18
2097144-43-7	Alkanes, C20-28, chloro	Active	0	0	No CID
2097144-45-9	Alkanes, C20-24, chloro	Active	0	0	No CID
2097144-46-0	Hexacosane, chloro derivs.	Active	0	0	No CID
2097144-47-1	Octacosane, chloro derivs.	Active	0	0	No CID
2097144-48-2	Octadecane, chloro derivs.	Active	0	0	No CID
24173-07-7	1,2,3,4-Tetrabromo-2,3-dimethylbutane	Not found	Not found	0	8
288260-42-4	Alkanes, C22-30, chloro	Active	0	0	No CID
3234-02-4	2,3-Dibromo-2-butene-1,4-diol	Not found	4	0	1,068
3296-90-0	Pentaerythritol dibromide	Active	3	5	968
36483-57-5	Tribromoneopentyl alcohol	Active	4	2	No CID
36678-45-2	2-Butene, 1,1,2,3,4,4-hexabromo-	Inactive	Not found	0	93
61788-76-9	Chloroalkanes	Active	4	1	1
63449-39-8	Chlorinated paraffins	Active	5	2	224
68527-01-5	Bromo chloro C12-30 a-alkenes	Active	2	0	No CID

[13] 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
68527-02-6	Alkenes, C12-24, chloro	Active	2	0	2
68920-70-7	Alkanes, C6-18, chloro	Active	3	1	No CID
68955-41-9	1-Bromo-4-chlorodecane	Inactive	Not found	1	1
71011-12-6	Alkanes, C12-13, chloro	Inactive	1	1	No CID
75-95-6	Pentabromoethane	Not found	Not found	0	574
79-27-6	1,1,2,2-Tetrabromoethane	Active	4	0	3,192
84082-38-2	C10-21, chloro	Not found	3	1	No CID
84776-06-7	Alkanes, C10-32, chloro	Not found	1	1	No CID
85049-26-9	Alkanes, C16-35, chloro	Not found	1	0	No CID
85422-92-0	Chlorinated paraffin oils	Not found	2	1	No CID
85535-84-8	C10-13 chloro alkanes	Not found	5	1	No CID
85535-85-9	Cercelor S 52 (MCCP)	Active	5	4	No CID
85535-86-0	C18-28 Chloroalkanes	Not found	1	1	No CID
85536-22-7	Alkanes, C12-14, chloro	Not found	1	1	No CID
85681-73-8	Chloroalkanes, C10-14	Not found	1	1	No CID
96-13-9	2,3-Dibromopropanol	Active	4	0	3,966
97553-43-0	Paraffins (petroleum), normal C>10, chloro	Not found	1	1	No CID
97659-46-6	Alkanes, C10-26, chloro	Not found	1	1	No CID

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

5.2.2. PHAChs Used in Consumer Products

The Market and Use Report identified the use of PHAChs 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,[14] 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 PHACh chemicals were also found in the literature.

Targeted Literature Search. In the literature, PHACs have been cited in the sources reviewed. Among the PHACs cited, chemicals appearing in the greatest number of these sources include CAS Nos. 3296-90-0 (5 sources), 85535-85-9 (4 sources) and 63449-39-8, 1522-92-5, 36483-57-5, and 108171-26-2 (2 sources each). No sources reported concentration data for any products in this class.

[14] 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.

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

- **CAS No. 108171-26-2**: polyvinyl chloride (PVC) plasticizers, paints, adhesives and sealants, leather fat liquors, and rubber/flame retardants/textiles/polymers (other than PVC).
- **CAS No. 3296-90-0**: rigid polyurethane foams and unsaturated polyester resins for molded products; polymers and thermoplastic manufacturing; building and construction materials.
- **CAS No. 36483-57-5**: rigid and flexible foams; thermoplastic resins, thermoset resins, textiles, adhesives, circuit boards, electronic enclosures, paper, thermal insulation for building applications.
- **CAS No. 63449-39-8**: plasticizers, additives in rubbers, plastics, paints, coatings, sealants, and adhesives.
- **CAS No. 71011-12-6**: PVC plasticizers, paints, adhesives and sealants, leather fat liquors, and rubber/flame retardants/textiles/polymers (other than PVC).
- **CAS No. 85535-85-9**: PVC plasticizers, paints, adhesives and sealants, leather fat liquors, and rubber/flame retardants/textiles/polymers (other than PVC).
- **CAS No. 85536-22-7**: PVC plasticizers, paints, adhesives and sealants, leather fat liquors, and rubber/flame retardants/textiles/polymers (other than PVC).
- **CAS No. 85681-73-8**: PVC plasticizers, paints, adhesives and sealants, leather fat liquors, and rubber/flame retardants/textiles/polymers (other than PVC).

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.[15] 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. 19 percent, or 206 reports, documented the use of PHACh chemicals in children's products.

Table 5-3 shows the two PHACh chemicals reported to be used in children's products. Of the 206 reported uses of PHAChs in children's products, 10 were for use as a chemical flame retardant. Of the 206 reported uses of PHAChs in children's products, most chemicals were reportedly used in trace amounts, although 78 reports identified the use of PHAChs in children's products in concentrations greater than 1,000 ppm (0.1%); levels below 0.1% are considered contaminant levels by CPSC staff.[16] There were four reported uses of PHAChs in concentrations greater than 0.1% that were expressly for use as a chemical flame retardant in a children's product.

[15] At this time, CPSC staff is unable to determine if information reported to the HPCDS for Washington and Oregon is representative. Presumably, the number of reports would go up 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.

[16] This amount corresponds with information on candidate list substances in articles for which importers and producers have to submit a SCIP 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.

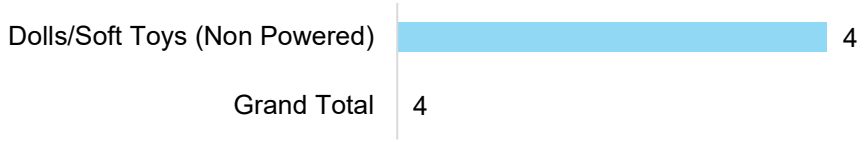
Table 5-3. Number of Children's Products with Reported Use as Flame Retardants for Select PHACh Chemicals

PHAChs	Total Report Count	Flame Retardant Use	Concentration >0.1%	Concentration >0.1% + FR Use
108171-26-2	43	6	10	2
85535-84-8	163	4	68	2
Total	**206**	**10**	**78**	**4**

Source: HPCDS, Interstate Chemicals Clearinghouse.

As shown in Figure 5-1, the four reported applications for which PHAChs are used as chemical flame retardants (in concentrations greater than 0.1%) were (non-powered) dolls and soft toys. (See Exhibit 3-28 in the Market and Use Report, Volume 1.)

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



Source: HPCDS, Interstate Chemicals Clearinghouse.

Among children's products identified to contain PHACh chemical FRs in a concentration greater than 0.1%, these high priority chemicals are 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 PHACh 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)
108171-26-2	C10-12 chloroalkanes	X	X
85535-84-8	C10-13 chloro alkanes	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 at least seven PHACh chemicals were included in the SCIP database. (See Exhibit 3-30 in the Market and Use Report, Volume 1.)

Table 5-5. PHACh Chemicals Included in SCIP Database

CAS RN	Substance Name	EC No.	Number of Search Results Returned
1372804-76-6	Alkanes, C14-16, chloro	NA	285
1522-92-5	3-Bromo-2,2-bis(bromomethyl)propanol	NA	679
3296-90-0	Pentaerythritol dibromide	221-967-7	42
36483-57-5	Tribromoneopentyl alcohol	253-057-0	24
85535-84-8	C10-13 chloro alkanes	287-476-5	2,310
85535-85-9	Cercelor S 52 (MCCP)	287-477-0	489,061
96-13-9	2,3-Dibromopropanol	202-480-9	51,216

As of May 2023, there were over 490,000 search results for PHACh chemicals in the SCIP database. Articles that contain this candidate list substance can be found in over 220 article categories that can be used to help identify articles based on function and use. According to SCIP data, PHACh chemicals can be found in products suitable for use as glues or adhesives, ridged and flexible tubes, pipes and hoses, plastic statuettes and other ornamental articles, protective face shields and visors, inflatable articles, woven fabrics of synthetic fibers, felt textiles, non-woven (man-made) textile materials, vehicle rearview mirrors, iron and steel articles and copper alloys, and hand tools (such as spades, shovels, and rakes). 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, PHACh 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 PHACh chemicals because CPSC needs to know the range of 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 PHACh chemicals in

[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.

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 PHACh chemicals are in products where the use description is not identified, paints and coatings, and in rubber and plastic products, although PHAChs are reported to be used in a variety of other products as well.

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

Product Use Category	2006	2012	2016	Total
Product description, not identified	2	1	10	**13**
Foam seating and bedding products	NR	1	1	**2**
Rubber and plastic products	1	2	3	**6**
Adhesives and sealants	1	1	NR	**2**
Electrical and electronic products	1	NR	NR	**1**
Floor coverings	NR	1	NR	**1**
Lubricants and greases	NR	NR	3	**3**
Paints and coatings	NR	3	4	**7**
Grand Total	**5**	**9**	**21**	**35**

Notes: Data listed as "Product description not identified" may be interpreted as one of any of the other product categories reported for PHAChs, 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 PHACh chemicals in children's products was not readily obtainable according to industry. In 2012, the use of PHACh chemicals in children's products was considered not known or reasonably ascertainable (NKRA). In 2016, the use of PHACh chemicals in children's products was also considered NKRA.

5.2.3. Regulatory History and Trends for PHAChs

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

[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.

[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.

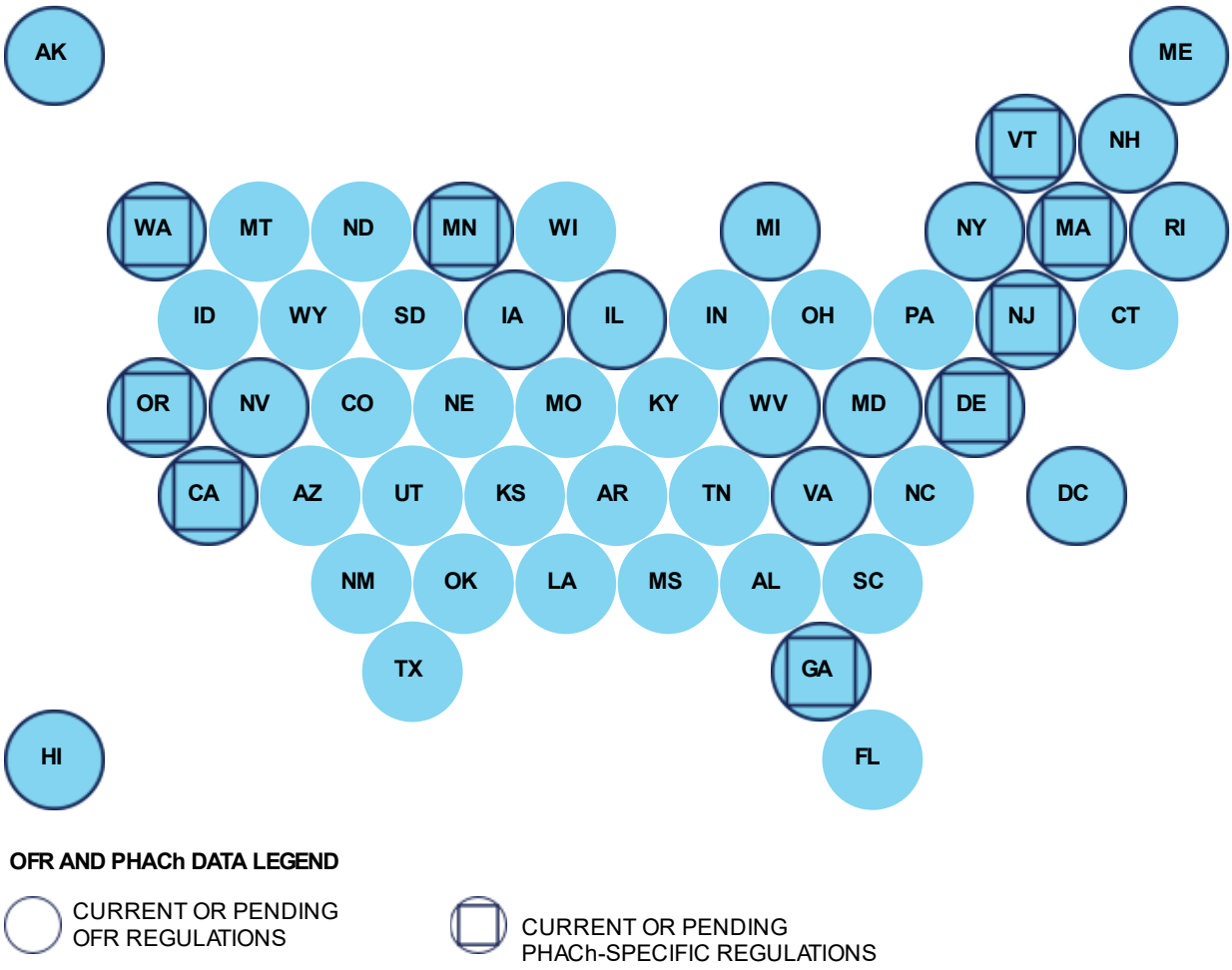
actions varies significantly. This section describes legislative actions taken in the United States at the state level.

The Market and Use Report provides greater detail of legislative action taken in the United States, as well as 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 chemicals regulations. State regulation of OFRs has tended to focus primarily on 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 regulated the use of OFRs, nine states currently regulate the use of PHAChs specifically or have regulations pending. In the map below (Figure 5-2), states that regulate OFRs or have pending regulations are shown with a circle border, and states that regulate PHAChs specifically or have pending PHACh-specific regulations are shown with a square within the circle. For more information on the state regulation of OFRs and PHAChs, see Volume 2 of the Market and Use Report, Appendix R.

[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.

Figure 5-2. U.S. States That Regulate the Use of OFR and PHACh 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 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.

The general observations from the Level 2, 3, and 3B reviews are:

- PHACh members pentaerythritol dibromide, C10-13 chloro alkanes, Chlorinated paraffins, and Cercelor S 52 (MCCP) had high numbers of toxicity data sources in most categories.
- PHACh members C10-13 chloro alkanes, Chlorinated paraffins, Cercelor S 52 (MCCP), and Long-chain chlorinated paraffins (LCCP) had representation across all toxicity categories for database and PDF reviews.
- The *QSAR, Read-across, Analog* category (QSAR = quantitative structure activity relationships) had broad representation with 4.76% of PHACh members and 88.8% of analogs having at least one data source at Level 3 review and similar representation at Level 3B.
- Lindane was the most data-rich analog across all toxicity categories.

5.3.1. Summary of Level 2

The "Integrated" tab of the evidence map file contains summed Level 2 toxicity data counts across PDF and database data.[22]

The literature survey identified integrated data sources (sum of databases and PDFs) for 20 of 21 PHACh members and for 288 of 312 analogs. The PHACh members with the most data sources were C10-13 chloro alkanes, Cercelor S 52 (MCCP), chlorinated paraffins, and pentaerythritol dibromide. Table 5-7 summarizes how many PHACh 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 "PHACh 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	
	PHACh Chemicals (n = 21)	Analog Chemicals (n = 312)
21+	4	6
6–20	7	11
1–5	9	271
0	1	24

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 tox 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 sample of 25 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 PHACh 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						
	PHACh Chemicals (n = 21)						
	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+	7	0	2	9	16	3	6
6–20	4	1	4	2	2	3	2
1–5	2	4	12	1	2	7	3
0	8	16	3	9	1	8	10

[23] See evidence map file "PHACh Level 3 Evidence Maps 12.2.22, Tab: TOX Integrated" and "PHACh 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 13 PHACh members and 39 analogs at Level 3 review. Thirteen PHACh members and 28 analogs had data in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail for nine subcategories: Acute Toxicity, Systemic or Repeated Dose Toxicity, Neurotoxicity, Carcinogenicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental Toxicity, Irritation, Sensitization, and Endocrine Disruption. CPSC staff observed the following:

- PHACh members C10-13 chloro alkanes and Cercelor S 52 (MCCP) had data sources for all subcategories except Neurotoxicity and Endocrine Disruption.
- PHACh member 1,1,2,2-tetrabromoethane had data sources for all subcategories except Sensitization and Endocrine Disruption.
- Acute Toxicity, Systemic or Repeated Dose Toxicity, and Mutagenicity/Genotoxicity were the subcategories with data sources for the highest number of PHACh members.
- Four analogs (lindane; 1,2-dibromoethane; bromoethane; and 1,2,3,4,5,6-hexachlorocyclohexane) had data sources in all but one subcategory.

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 PHACh Analogs (n = 312)						
	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+	8	3	4	37	86	6	7
6–20	6	3	4	13	5	4	4
1–5	25	2	65	17	186	25	18
0	273	304	239	245	35	277	283

Human Toxicity data sources were available for five PHACh members and eight analogs at Level 3 review. Four PHACh members and seven analogs had data in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail for the same nine subcategories used for *Animal Toxicity or Accepted Alternative* above. CPSC staff observed the following:

- PHACh member C10-13 chloro alkanes had one or two data sources in subcategories Systemic or Repeated Dose Toxicity, Carcinogenicity, and Sensitization.
- PHACh members 1,1,2,2-tetrabromoethane and Cercelor S 52 (MCCP) had two data sources in the Systemic or Repeated Dose Toxicity subcategory.
- PHACh member chlorinated paraffins had a data source in the Carcinogenicity subcategory.
- Analog lindane had data sources in all subcategories except Irritation and Sensitization.
- Subcategories Systemic or Repeated Dose Toxicity, Reproductive Toxicity/Developmental Toxicity, and Endocrine Disruption each had data sources for at least five analogs.

Human, Animal, or Modeled Toxicokinetics (ADME [absorption, distribution, metabolism, and excretion]*)* data sources were available for 18 PHACh members and 73 analogs at Level 3 review and in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail on seven subcategories: Human Absorption, Distribution, Excretion; Animal Absorption, Distribution, Excretion; Human Metabolism; Animal Metabolism; In Vitro; Chemical or Class-Specific physiologically based pharmacokinetic (PBPK) Model; and Chemical- or Class-Specific QSAR for an ADME Parameter. CPSC staff observed the following:

- No data sources were reported for any PHACh members or analogs under the subcategory Chemical- or Class-Specific PBPK Model.
- PHACh members C10-13 chloro alkanes and Cercelor S 52 (MCCP) had data sources in subcategories Human Absorption, Distribution, Excretion; Animal Absorption, Distribution, Excretion; Animal Metabolism; and In Vitro.
- Fifteen PHACh members and 73 analogs had data sources in the Chemical- or Class-Specific QSAR for an ADME Parameter subcategory.
- The analog lindane had data sources in all subcategories.

Experimental Mechanistic data sources were available for 12 PHACh members and 67 analogs at Level 3 review. Nine PHACh members and 18 analogs had data in the databases and 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 PHACh members had data sources in both subcategories. These were pentaerythritol dibromide; 1,1,2,2-tetrabromoethane; and C10-13 chloro alkanes.

QSAR, Read-Across, Analog data sources were available for 20 PHACh members and 277 analogs at Level 3 and in the databases and PDFs 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:

[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.

- No data sources for PHACh members or analogs were identified for Neurotoxicity. Most data with the *QSAR, Read-across, Analog* tag are from the Danish QSAR Database, which does not include any data that are taggable as Neurotoxicity.
- Of the remaining subcategories, at least one data source was available for 13 to 18 PHACh members per subcategory.
- The subcategories Acute Toxicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental Toxicity, and Endocrine Disruption had data sources for the majority of analogs.

Qualitative Hazard Characterization data sources were available for 13 PHACh members and 35 analogs at Level 3 review. Twelve PHACh members and 35 analogs had data in the databases and PDFs at Level 3B review. In contrast with all other data types, a tag for Qualitative Hazard Characterization indicates that a review/assessment was attempted, not necessarily that data were found (e.g., if a review/assessment clearly stated that authors looked for data for endpoint X for chemical Y but found none, chemical Y was tagged for Qualitative Hazard Characterization for endpoint X, but not as any other data type.) This category was separated into the same nine subcategories used for *Animal Toxicity or Accepted Alternative* above for Level 3B review. CPSC staff observed the following:

- PHACh members pentaerythritol dibromide; 1,1,2,2-tetrabromoethane; 2,3-dibromopropanol; and 1-chlorooctane had data sources in all subcategories except Endocrine Disruption.
- Subcategories Acute Toxicity and Mutagenicity/Genotoxicity had data sources for the highest numbers of PHACh members and analogs.
- Analogs 1,2-dibromoethane; 1,2,3,4,5,6-Hexachlorocyclohexane; and lindane had data sources for all nine subcategories.

Quantitative Hazard Characterization data sources were available for 11 PHACh members and 29 analogs at Level 3 review. Eleven PHACh members and 30 analogs had data in the databases and PDFs 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 Toxicity, Sensitization, and Endocrine Disruption. CPSC staff observed the following:

- No data sources for PHACh members were identified for subcategories Neurotoxicity and Sensitization.
- PHACh members C10-13 chloro alkanes and Cercelor S 52 (MCCP) had data sources in the remaining subcategories.
- Subcategories Acute Toxicity and Systemic or Repeated Dose Toxicity had data sources for eight to nine PHACh members and 11 to 20 analogs.
- Analog 1,2,3,4,5,6-hexachlorocyclohexane had data sources in all subcategories.
- Analog lindane had data sources in all subcategories except Sensitization.

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 25 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 the individual PDF file. PHACh 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 are:

- PHACh member C10-13 chloro alkanes had the highest number of data sources in each category.
- PHACh members C10-13 chloro alkanes and Cercelor S 52 (MCCP) had the most representation across exposure categories for database and PDF reviews.
- Most (85.7%) PHACh members had Source Characterization data.

5.4.1. Summary of Level 2

The MMDB database and PDF searches identified exposure data sources for 18 of 21 PHACh members.[27] The PHACh members with the most data sources were C10-13 chloro alkanes, Cercelor S 52 (MCCP), and chlorinated paraffins. Table 5-10 summarizes how many PHACh members had different degrees of data source abundance. The PDFs provided more total data sources and covered more PHACh members than the database.

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 PHACh Chemicals (n = 21)
21+	4
6–20	2
1–5	12
0	3

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 selected

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

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 PHACh members had different degrees of Level 3 exposure data source abundance.

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 PHACh Chemicals (n = 21)					
	Environmental Monitoring	Biomonitoring/ Personal Monitoring	Source Characterization	Epidemiology – Population Group	Modeled Concentrations	Modeled Human Dose
21+	2	1	4	0	0	1
6–20	2	3	2	0	2	2
1–5	4	2	12	2	3	1
0	13	15	3	19	16	17

Environmental Monitoring data sources were available for eight PHACh members at Level 3 review. Six PHACh members had data in the database and 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.

- PHACh members C10-13 chloro alkanes and Cercelor S 52 (MCCP) had sources in all six subcategories.
- PHACh member C10-13 chloro alkanes had 15,936 data sources for Drinking Water.
- PHACh member chlorinated paraffins had data sources in Indoor Dust, Outdoor Air, Food/Dietary, and Soil.
- PHACh member chloroalkanes had one data source each for Outdoor Air, Food/Dietary, and Soil.
- PHACh member 2,3-dibromopropanol had one data source for Indoor/Personal Air and Indoor Dust.
- PHACh member Long-chain chlorinated paraffins (LCCP) had one data source for Food/Dietary.

Biomonitoring/Personal Monitoring data sources were available for six PHACh members at Level 3 review and in the database and 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).

- PHACh members C10-13 chloro alkanes, Cercelor S 52 (MCCP), and chlorinated paraffins had data sources in the Blood/Serum, Breast Milk/Lipids, and Human (Other) subcategories.
- PHACh member long-chain chlorinated paraffins (LCCP) had one data source each in the Blood/Serum and Breast Milk/Lipids subcategories.
- PHACh member 2,3-dibromopropanol had one data source for Blood/Serum.
- PHACh member chloroalkanes had one data source for Urine.

Source Characterization data sources were available for 18 PHACh members at Level 3 review. Fifteen PHACh members had data in the database and 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.

- No PHACh members had data sources for the Product Testing: Content Only or Product Testing: Emission/Migration Data subcategories.
- PHACh members C10-13 chloro alkanes, pentaerythritol dibromide, chlorinated paraffins, 2,3-dibromopropanol, pentabromoethane, Cercelor S 52 (MCCP), tribromoneopentyl alcohol, and long-chain chlorinated paraffins (LCCP) had data sources in the Nonexperimental Product- or Chemical-Specific Modeling Inputs and Other Qualitative or Quantitative Description of Product Use or Class/Chemical subcategories.
- PHACh members 2,3-dibromo-2-butene-1,4-diol; 1-propanol, 3,3'-oxybis[2,2-bis(bromomethyl)-; hexabromohexane, 2-butene; 1,1,2,3,4,4-hexabromo-; and chloroalkanes had at least one data source for the subcategory Other Qualitative or Quantitative Description of Product Use or Class/Chemical.
- PHACh members 3-Bromo-2,2-bis(bromomethyl)propanol and 1,1,2,2-Tetrabromoethane each had one data source for the Nonexperimental Product- or Chemical-Specific Modeling Inputs subcategory.

Environmental Epidemiology[29] data sources were available for two PHACh members at Level 3 review and in the database and PDFs at the Level 3B review. The subcategories were Children; Adult, Non-Occupational; and Other, Specify (with Suggestions).

- PHACh members C10-13 chloro alkanes and Cercelor S 52 (MCCP) had one data source each in the Adult, Non-Occupational subcategory.
- No PHACh members had data sources for the Children; Adult, Non-Occupational or Other, Specify (with Suggestions) subcategories.

Modeled Concentrations data sources for five PHACh members were identified at Level 3 review. Two PHACh members had data in the database and PDFs at Level 3B review. The subcategories were (Indoor Concentration, Outdoor Concentration, and Dietary/Food).

[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.

- PHACh member C10-13 chloro alkanes had data sources in the Outdoor Concentration and Dietary/Food subcategories.
- PHACh member Cercelor S 52 (MCCP) had data sources in the Dietary/Food subcategory.
- No PHACh members had data sources for the Indoor Concentration subcategory.

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

- PHACh members C10-13 chloro alkanes, Cercelor S 52 (MCCP), and long-chain chlorinated paraffins (LCCP) had data sources for the subcategories Children and Adult, Non-occupational.
- PHACh member chlorinated paraffins had two hits for Adult, Non-occupational.
- The subcategory Other, Specify (with Suggestions) had no hits for any PHACh members.

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.[30] No risk data were found in the databases. Four PHACh members and six analogs had PDF data sources for risk at Level 2 review. Table 5-12 summarizes how many PHACh members had different degrees of data source abundance. PHACh member C10-13 chloro alkanes had the highest numbers of human health risk assessments available.

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 Level 2 Risk Data Sources	
	PHACh Chemicals (n = 21)	Analog Chemicals (n = 312)
21+	1	4
6–20	1	1
1–5	2	1
0	17	306

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

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 25 PDFs that were selected for 3B extraction. The counts indicate the number of PDFs identified per chemical for each Noncancer and Cancer risk assessment. Table 5-13 summarizes how many PHACh members and analogs had different degrees of Level 3 human health risk data source abundance.

Table 5-13. Distribution of Human Health Risk Data Sources Abundance Levels at Level 3

Distribution of Number of Data Sources Available for Each Chemical	Number of Chemicals with Level 3 Risk Data Sources	
	PHACh Chemicals (n = 21)	Analog Chemicals (n = 312)
21+	1	4
6–20	1	1
1–5	2	1
0	17	306

Human Health Risk Assessment data were available for four PHACh members and six analogs at Level 3 review. Three PHACh members and four analogs had data in the selected PDFs at Level 3B review. The subcategories used were Noncancer Risk and Cancer Risk. Staff noted the following observations:

- No PHACh members or analogs had Cancer Risk data sources.
- PHACh member C10-13 chloro alkanes had five Noncancer Risk data sources.
- PHACh member Cercelor S 52 (MCCP) had three Noncancer Risk and one Cancer Risk data sources.
- PHACh member Long-chain chlorinated paraffins (LCCP) had one Noncancer Risk data source.
- Four analogs (lindane; 1,2,3,4,5,6-hexachlorocyclohexane; beta-hexachlorocyclohexane; and alpha-1,2,3,4,5,6-Hexachlorocyclohexane) had one to three Noncancer Risk data sources each.

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 (ASTDR), European Chemicals Agency (ECHA) Reports, International Agency for Research on Cancer (IARC) evaluations, National Toxicology Program (NTP) technical reports, Organisation for Economic Cooperation and Development (OECD) assessments and U.S. Environmental Protection Agency (EPA) reviews and assessments. Each of these references

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

addressed one or more PHAChs.[32] These reports included seven PHAChs and eight PHACh analogs. The seven PHACh chemicals are among the PHAChs most frequently noted in the market use report as found in consumer products, as well as in the literature survey results generally. These reports demonstrate the existence of data about these chemicals, including hazard and potential exposures, that are sufficient to support hazard, exposure, and risk assessment, and are likely to be useful references for CPSC staff evaluations of these and other PHAChs.

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 PHACh 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 PHACh 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 PHACh subclass includes seven data-rich PHACh chemicals and six data-rich analogs. A majority of PHACh chemicals and some analogs have some data. The evidence maps show that many PHACh 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 PHACh 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 seven data-rich chemicals and that a majority of chemicals have some data. In addition, according to available data sources, 42 of the 47 chemicals have market information for use in commerce.

Following the determination that the PHACh 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

[32] The seven PHAChs included in one or more key references are (by CAS RN): 85535-85-9; 85535-84-8; 96-13-9 ; 63449-39-8; 3296-90-0; 85535-86-0; 85422-92-0. The eight PHACh analogs included in one or more of the key references are (by CAS RN): 58-89-9; 319-84-6; 319-85-7; 319-86-8; 608-73-1; 6108-10-7; 106-93-4; 3386-33-2.

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 PHACh 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 PHAChs, data-rich PHACh analogs, PHAChs with some toxicity information, and PHAChs 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][33]) from the comprehensive literature search.
3. CPSC staff will refine the NAS analog list and characterize analog substances for the PHACh class that are both chemically and toxicologically similar and have any amount of empirical toxicity information. Analog substances that are data poor, and not sufficiently similar to PHACh class members to be associated with them, will be deprioritized. CPSC staff's initial survey shows that empirical toxicity data are available for 39 analogs and empirical toxicokinetic data are available for 73 analogs.
4. CPSC staff will estimate major metabolites of PHACh 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 PHACh class members and analogs with available toxicity data can be used to read-across to PHACh 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 PHACh class are acute toxicity, systemic

[33] 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.

repeat dose toxicity, carcinogenicity, reproductive toxicity/developmental toxicity, and mutagenicity/genotoxicity.

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 PHACh 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 PHACh class members.
8. CPSC staff will explore the variability and uncertainty associated with dose response values for PHACh 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 PHAChs.

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

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.

Acute oral toxicity is low for CPs (LD50s > 4,000 mg/kg; EFSA, 2020), and low but somewhat higher for DBNPG (LD50s > 2,810 mg/kg; NTP, 1996b). No acute oral studies for 2,3-dibromopropanol were identified, but intraperitoneal (IP) injection of 200 mg/kg killed all rats within 24 hours, and the IP LD50 for mice was 125 mg/kg (NTP, 1993). In a 21-day gavage study, all rats administered 0.21 or 0.43 mg/kg/day of 1,1,2,2-tetrabromoethane died by day 11, and all rats administered 0.53 mg/kg/day of pentabromoethane died by the end of the study (NTP, 1996a).

The kidney has been identified as a target of SCCPs and MCCPs (EFSA, 2020) and pentabromoethane (NTP, 1996a). CPs (including SCCPs, MCCPs, and LCCPs) have also been found to affect the liver, and SCCPs and MCCPs have been found to affect the thyroid (EFSA, 2020). DBNPG (NTP, 1996b) and SCCPs (EFSA, 2020) have caused developmental/reproductive effects, a target for which MCCPs have conflicting findings (EFSA, 2020). An MCCP caused vitamin K deficiency and disrupted clotting in lactating rat pups of treated dams (EFSA, 2020).

Mechanistic data were identified for CPs and pentabromoethane. SCCPs can cause liver tumors in rodents via CAR and PPARα activation, but this mechanism does not appear to be relevant to humans in the absence of cytotoxicity (EFSA, 2020). In liver cells in vitro, SCCPs and MCCPs affected fatty acid metabolism (Ding et al., 2020; Zheng et al., 2020), and SCCPs

altered steroid hormone production (Ding et al., 2020), glycolysis, and amino acid metabolism (Wang et al. 2021). SCCPs can also cause kidney tumors in male rats, as a result of nephropathy (partially but possibly not exclusively related to α2-microglobulin, a MOA that is not relevant to humans) and regenerative hyperplasia (EFSA, 2020). Pentabromoethane exposure increased replicative DNA synthesis in rat kidneys, without hyaline droplet nephropathy (NTP, 1996a). CPs also induced changes in thyroid hormones and cancer in rodents (EFSA, 2020).

These thyroid hormone effects in male animals resulted from stimulation of the thyroid via a negative feedback mechanism that is relevant to humans for developmental neurotoxicity but not carcinogenesis (Dellarco et al., 2006; EFSA, 2020), though clear evidence on developmental neurotoxicity of CPs was not identified (EFSA, 2020). Thyroid effects in female animals could not be clearly eliminated for human relevance (EFSA, 2020).

PHACh subclass members were generally negative or had mixed results for genotoxicity, though TBNPA, DBNPG, and 2,3-dibromopropanol have isolated positive results. EFSA (2020) concluded CPs are not genotoxic as a whole, based on negative results in bacterial (SCCPs, MCCPs, LCCPs) and rat (SCCP) gene mutation assays, in vivo chromosomal aberration studies (SCCPs, MCCPs, LCCPs), mouse micronucleus tests (SCCPs, MCCPs), and rat germ cell mutagenicity assays (SCCPs); however, positive results were seen in an in vitro mouse lymphoma test (SCCPs) and a chromosomal aberration study (LCCPs). TBNPA was mutagenic in the Ames test only in the presence of atypical (hamster S9) metabolic activation and is suspected of causing genetic defects via germ cell mutagenicity (Danish EPA, 2014). DBNPG had mixed results in in vivo micronucleus assays, caused chromosomal aberrations in vitro only in the presence of S9 activation, and had mixed results in bacterial gene mutation assays (NTP, 1996b). 2,3-dibromopropanol had positive results in mouse lymphoma gene mutation and chromosomal aberration assays (with and without S9 activation), but mixed results in bacterial gene mutation assays (NTP, 1993). 1,1,2,2-tetrabromoethane was negative in bacterial mutagenicity tests (NTP, 1996a).

IARC classified SCCPs as a Group 2B carcinogen (possibly carcinogenic to humans) but did not assign an IARC group to LCCPs (IARC, 1990; EFSA, 2020). NTP classified SCCPs as “reasonably anticipated to be human carcinogens,” and reported mixed results of animal carcinogenicity studies for LCCPs (no evidence in male rats, clear evidence in male mice, and equivocal evidence in female rats and female mice; EFSA, 2020). EFSA (2020) did not identify any carcinogenicity studies on MCCPs. Both DBNPG (NTP, 1996b) and 2,3-dibromopropanol (NTP, 1993) have clear evidence of causing cancer in male and female rats and mice. Shared tumor sites were liver (SCCP, LCCP, 2,3-dibromopropanol), kidney (SCCP, 2,3-dibromopropanol, DBNPG), and thyroid (SCCP, DBNPG) (EFSA, 2020; NTP, 1996b; NTP, 1993). 2,3-dibromopropanol and DBNPG both caused tumors in skin, in various locations in the gastrointestinal tract, and Zymbal’s gland (NTP, 1996b; NTP, 1993).

Overall, there may be enough information for a class-based assessment including some PHACh subclass members, though careful consideration of the relevance of mechanisms is warranted. Carcinogenicity may be a shared endpoint of SCCPs, DBNPG, and 2,3-dibromopropanol. Kidney and reproductive/developmental effects may be worth further investigation to connect some CPs to other subclass members, though insufficient detail was identified to this point. One challenge for this class will be integrating the multiple ways in which data on CPs are reported.

Data may be reported for CPs as a group, for SCCPs or MCCPs or LCCPs as groups, for specific chemicals within each of these groups, or for particular carbon chain lengths and/or degrees of chlorination.

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 PHACh class members will be further summarized and integrated after this search is complete. After the search, staff will refine the list of data-rich PHACHs, PHACHs with some exposure and use information, and PHACHs with no exposure and use information.
2. Using the market and use research, CPSC staff expects to compile a list of PHACh chemicals that have been or could be used in consumer products. While 42 of the 47 chemicals had some market-use information, 20 PHACh chemicals had more market and use information that could be used to inform analyses for PHACh chemicals with less information. CPSC staff will characterize uses for PHACHs 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 20 and 42 PHACh subclass members.
4. Exposure pathways with likely higher potential for PHACh class members include dietary ingestion, drinking water ingestion, contact exposures with consumer products and articles, indoor dust ingestion, and inhalation of indoor air. Exposure pathways with likely lower potential for PHACh class members include ambient air 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 18 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 PHACh 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

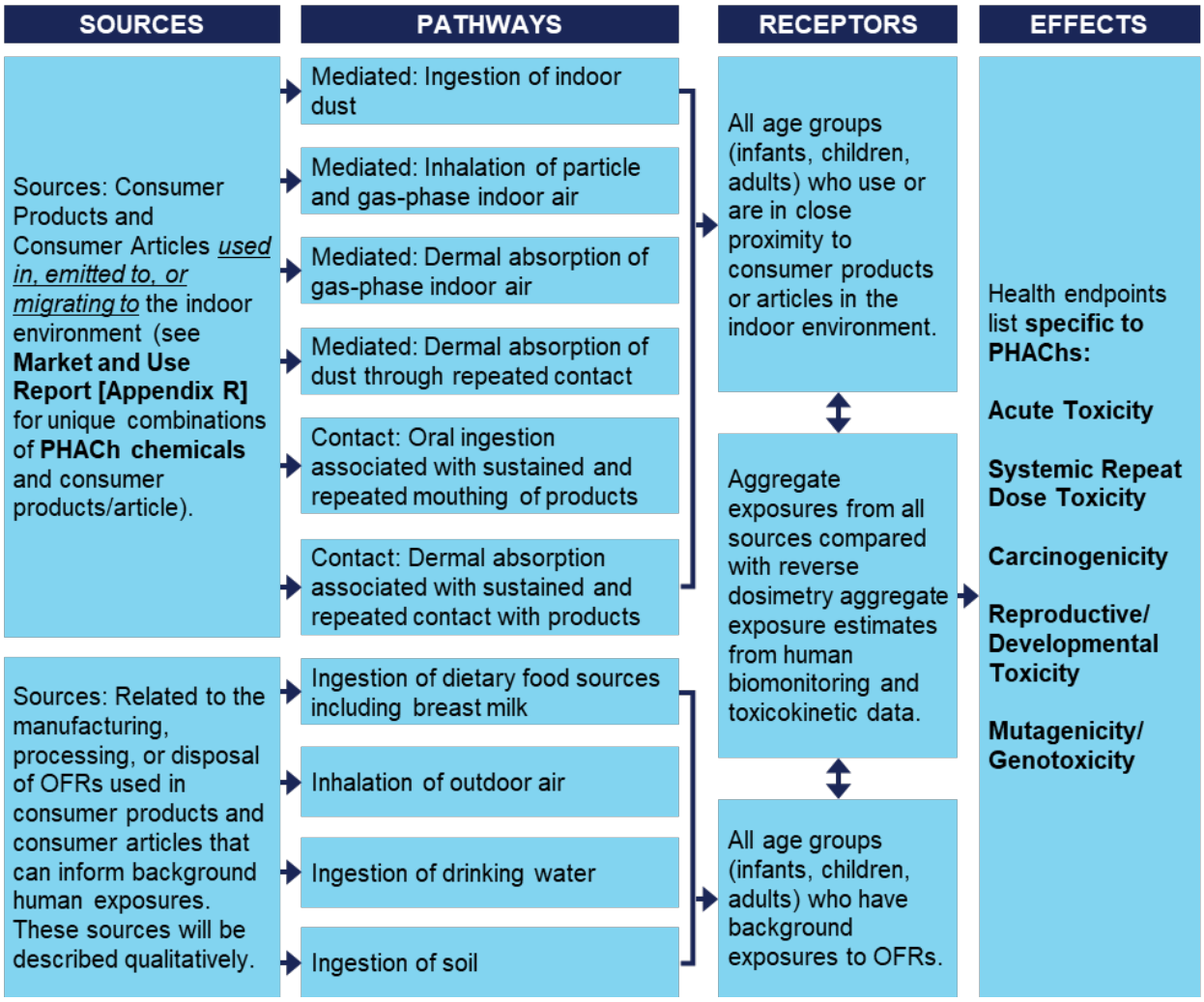
uses and determining whether these estimates fall within the range of reported environmental monitoring data. CPSC staff plans to consider indoor exposure modeling, modeling approaches specific to semi-volatile organic compounds (SVOCs), and product-testing measurement techniques that characterize emissions 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 10 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 six PHACh 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 PHAChs.

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 PHACh 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 PHAChs are listed.

Figure 6-1. PHACh 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. *Scientific Data, 9*, Article 295. https://doi.org/10.1038/s41597-022-01351-0

Consumer Product Safety Commission (CPSC). (2020). *Staff briefing package: Project plan: Organohalogen flame retardant chemicals assessment: July 1, 2020*. https://www.cpsc.gov/s3fs-public/OFR-plan-report-package-final.pdf

Danish Environmental Protection Agency (Danish EPA). (2014). *Survey of brominated flame retardants: Part of the LOUS-review* (Environmental Project No. 1536). https://www2.mst.dk/udgiv/publications/2014/01/978-87-93026-90-2.pdf

Dellarco, V.L., McGregor, D., Berry, S.C., Cohen, S.M., & Boobis, A.R. (2006). Thiazopyr and thyroid disruption: Case study within the context of the 2006 IPCS Human Relevance Framework for analysis of a cancer mode of action. *Critical Reviews in Toxicology, 36*(10), 793-801. https://doi.org/10.1080/10408440600975242

Ding, L., Luo, N., Liu, Y., Fang, X., Zhang, S., Li, S., Jiang, W., & Zhao, N. (2020). Short and medium-chain chlorinated paraffins in serum from residents aged from 50 to 84 in Jinan, China: Occurrence, composition and association with hematologic parameters. *Science of the Total Environment, 728*, Article 137998. https://doi.org/10.1016/j.scitotenv.2020.137998

EFSA Panel on Contaminants in the Food Chain (CONTAM), Schrenk, D., Bignami, M., Bodin, L., Chipman, J.K., del Mazo, J., Grasl-Kraupp, B., Hogstrand, C., Hoogenboom, L., Leblanc, J.C., Nebbia, C.S., Ntzani, E., Petersen, A., Sand, S., Schwerdtle, T., Vleminckx, C., Wallace, H., Brüschweiler, B., Leonards, P., Rose, M., Binaglia, M., Horváth , Z., Bordajandi, L.R., & Nielsen, E. (2020). Scientific opinion: Risk assessment of chlorinated paraffins in feed and food. *EFSA Journal, 18*(3), Article 5991. https://doi.org/10.2903/j.efsa.2020.5991

International Agency for Research on Cancer (IARC). (1990). Chlorinated paraffins (group 2B). In *Summaries & evaluations* (Vol. 48, p. 55). International Programme on Chemical Safety. https://inchem.org/documents/iarc/vol48/48-02.html

National Academies of Sciences, Engineering, and Medicine (NASEM). (2019). *A class approach to hazard assessment of organohalogen flame retardants*. The National Academies Press. https://doi.org/10.17226/25412

National Toxicology Program (NTP). (1993). *NTP technical report on the toxicology and carcinogenesis studies of 2,3-dibromo-1-propanol (CAS No. 96-13-9) in F344/N rats and B6C3F1 mice (dermal studies)* (NTP TR 400). U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. https://ntp.niehs.nih.gov/go/tr400abs

National Toxicology Program (NTP). (1996a). *NTP technical report on renal toxicity studies of selected halogenated ethanes administered by gavage to F344/N Rats* (Toxicity Report Series Number 45). U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. https://ntp.niehs.nih.gov/go/tox045abs

National Toxicology Program (NTP). (1996b). *NTP technical report on the toxicology and carcinogenesis studies of 2,2-bis(bromomethyl)-1,3-propanediol (FR-1138®) (CAS No. 3296-90-0) in F344/N rats and B6C3F1 mice (feed studies)* (NTP TR 452). U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health. https://ntp.niehs.nih.gov/go/tr452abs

University of Cincinnati (UC). (2022a). *Literature survey guide: Draft 6: October 17, 2022.* Prepared by Risk Science Center, Department of Environmental and Public Health Science, University of Cincinnati under contract with the U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022b). *Screener guide for class-based OFR literature surveys: April 5, 2022*. Prepared by Risk Science Center, Department of Environmental and Public Health Science, University of Cincinnati under contract with the U.S. Consumer Product Safety Commission.

Wang, M., Gao, Y., Li, G., & An, T. (2021). Increased adverse effects during metabolic transformation of short-chain chlorinated paraffins by cytochrome P450: A theoretical insight into 1-chlorodecane. *Journal of Hazardous Materials, 407*, Article 124391. https://doi.org/10.1016/j.jhazmat.2020.124391

Zheng, X., Sun, Q., Wang, S., Li, X., Liu, P., Yan, Z., Kong, X., & Fan, J. (2020). Advances in studies on toxic effects of short-chain chlorinated paraffins (SCCPs) and characterization of environmental pollution in China. *Archives of Environmental Contamination and Toxicology, 78*, 501-512. https://doi.org/10.1007/s00244-020-00723-0

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.

Literature Survey Guide: Approaches Taken to Develop Evidence Maps from Readily Available Databases, Completed Assessments, and Literature Reviews

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 Report: Characterizing OFR Chemistries, Sources, and Uses in the U.S. and International Markets, Volumes 1 and 2 (Appendices)

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.

Literature Survey Results

University of Cincinnati (UC). (2022). *PHACh subclass level 2 literature survey evidence map* [PHACh Level 2 Evidence Maps 12.7.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass level 3 literature survey evidence map* [PHACh Level 3 Evidence Maps 12.7.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass level 3B literature survey evidence map* [PHACh Level 3B Evidence Maps 12.7.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass information downloaded from databases* [PHACh Tox Individual Database Evidence Maps - Levels 2, 3, 3B - 12.7.22.xlsx]. U.S. Consumer Product Safety Commission.

Literature Survey Results Supporting Files

University of Cincinnati (UC). (2022). *PHACh subclass detailed 3B extraction counts* [PHACh PDF 3B Extraction Final 11.22.22.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass selected studies for 3B extraction* [PHACh 3B Selection Sheets.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass information and heatmaps for level 3B study selection* [PHACh 3B Selection Heatmaps.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass power-query cleaning and visualizing of PDF data sources* [PHACh PQ clean and viz.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass data from Multimedia Monitoring Database* [PHACh MMDB All Levels.xlsx]. U.S. Consumer Product Safety Commission.

University of Cincinnati (UC). (2022). *PHACh subclass aggregated toxicity database counts* [PHACh DB Tox Totals All Levels.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.

Eastern Research Group Incorporated (ERG). (2022). *Market research source list* [02_SourcesList_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Market research TSCA inventory* [OFR_universe_wTSCA_03042022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Organohalogen flame retardant (OFR) market data workbook* [_OFR Market Data Workbook_mod1_01.25.2022.xlsx]. U.S. Consumer Product Safety Commission.

Eastern Research Group Incorporated (ERG). (2022). *Organohalogen flame retardant (OFR) source extraction workbook* [OFR Source Review Workbook_mod1_02.28.2022.xlsx]. U.S. Consumer Product Safety Commission.