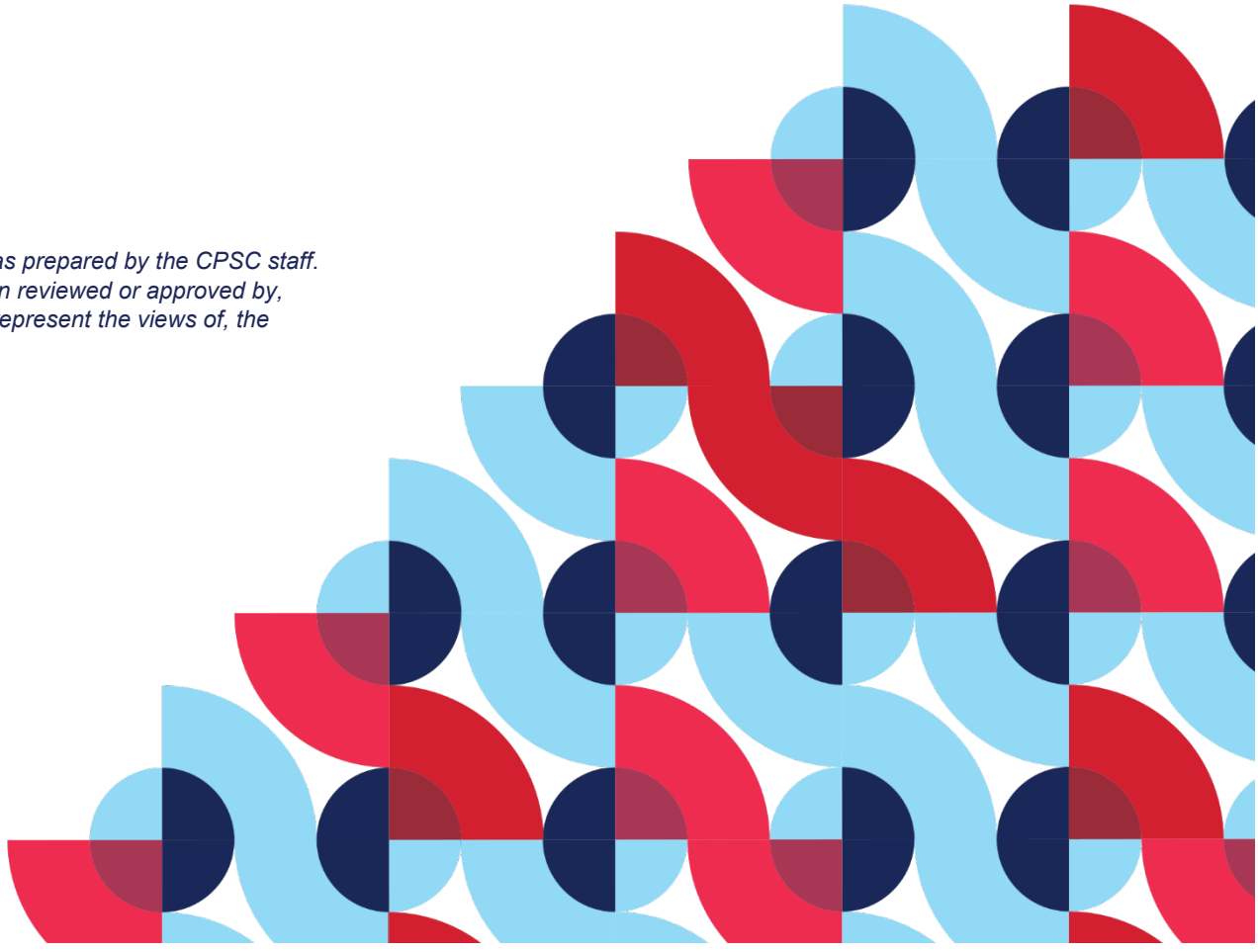
United States
Consumer Product Safety Commission

Organohalogen Flame Retardant Scope Document: Polyhalogenated Organophosphate Subclass

August 2023

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



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1. Executive Summary

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

Informed by initial review of the market and use research, evidence maps, and availability of physicochemical data for the PHOP 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 PHOP 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 PHOP subclass of OFRs. This document is one of the scope documents that CPSC staff is producing to address each of 14 OFR chemical subclasses.

The primary question answered by the scope documents is:

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

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

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

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

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

3. Background

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

NASEM established a committee of experts to address the charge and published the Committee's report, "A Class Approach to Hazard Assessment of Organohalogen Flame Retardants," in May 2019 (NASEM, 2019). The Committee first decided to determine whether the chemicals of interest can be defined as a single class or as subclasses, based on structure, physicochemical properties, biology, or a combination of characteristics. The Committee stated that if a class approach is viable, then the hazard assessment approach would be to survey the literature to determine availability of all types of toxicity data (human, animal, in vitro, other relevant studies) for all relevant toxicity end points. Then, if relevant data are available on any chemical of interest for a given end point, the plan would be to extract, evaluate, and integrate the data to reach a decision about potential hazards that can be applied to the entire class or subclass. 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,

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

the Staff Plan outlined work that initially would establish procedures for class-based risk assessment of each OFR subclass, refine the chemicals and analogs for multiple OFR subclasses, identify data sources, and determine available toxicity, chemical use, and exposure information. Staff subsequently initiated several activities, largely through contractors and interagency collaborations, to begin work on the project.

4. Approach

4.1. Criteria for Scoping Determination

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

4.1.1. Hazard

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

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

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

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

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

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

4.1.2. Exposure

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

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

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

- Chemicals with no data:
    - No market and use information indicating use as a flame retardant.

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

[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.

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. In addition to determining whether OFR substances appear as active substances on the TSCA chemical inventory, the contractor conducted a detailed analysis of U.S. production and import activity using data available from the EPA Chemical Data Reporting (CDR) program, and the manufacturing, processing, and waste management trends of OFR substances from the Toxic Release Inventory (TRI), as reported by industrial and federal facilities.

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

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

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

4.4. Literature Survey

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

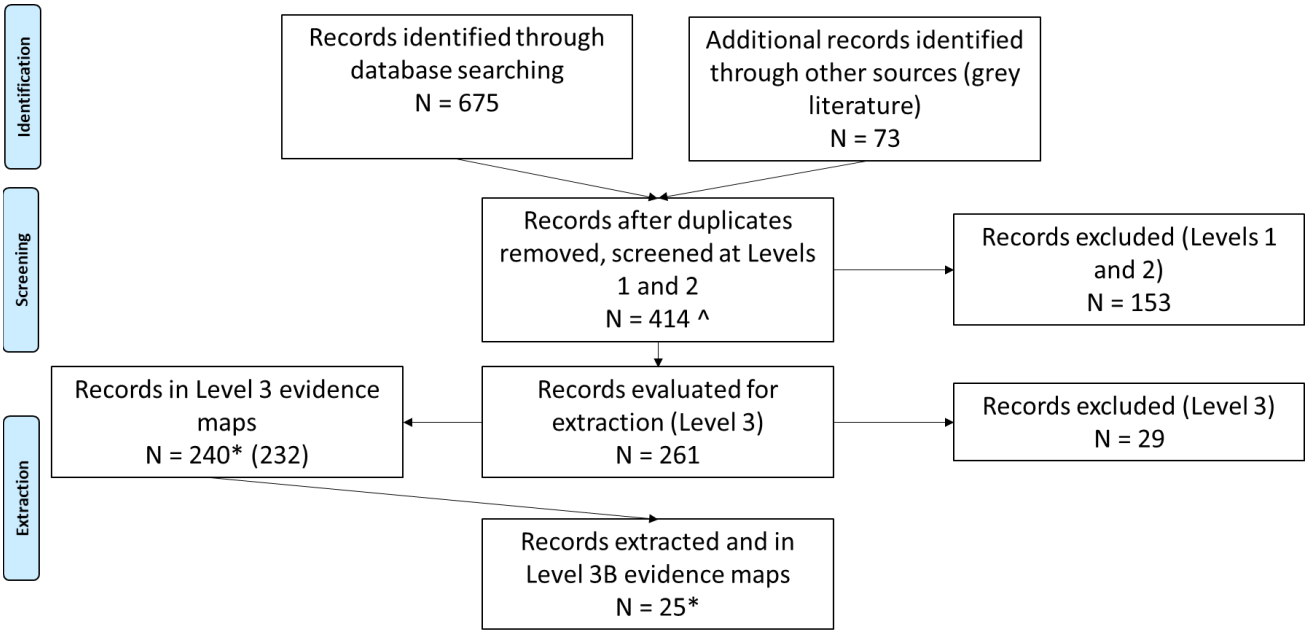
Detailed descriptions of the literature survey approach and process are found in the Literature Survey Guide and accompanying documentation. These documents were developed by University of Cincinnati (UC) Risk Science Center staff as part of work performed under a CPSC-sponsored contract (UC, 2022a;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

Briefly, for peer-reviewed and gray literature, **Level 1** screening was used to confirm that the reference might contain information about at least one OFR chemical and that the reference was relevant to the PECO statement.[10] **Level 2** screening identified the OFR subclasses included in each reference and tagged the references for the types of data (hazard, exposure, risk). **Level 3** identified the specific OFR or analog chemicals in each reference and extracted more specific information about the types of hazard data, exposure data, or risk assessment information presented for each chemical. Finally, **Level 3B** tagging was performed on a subset of toxicity assessments, toxicity literature reviews, risk assessments, and exposure literature reviews selected from Level 3 to identify even more specific information for the chemicals in these references.

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

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

Figure 4-1. Literature Flow Diagram



Notes:
^Removal of duplicates within the subclass.
*PHOP evidence maps contain additional references that were identified in the literature search for the polyhalogenated bisphenol aliphatic and functionalized (PHBAF) subclass. Number in parentheses is the number of references identified by searching for the PHOP subclass only, excluding the references identified by searching for PHBAFs.

5. Scoping for PHOPs

5.1. PHOP Subclass Chemistry

The PHOP subclass generally consists of chemicals containing an organophosphate (OP) functional group with halogenated alkyl or aryl substituents. Members of this subclass all have a phosphorus-oxygen double bond (P=O) or a phosphorus-oxygen single bond (P-O). The different oxidation states of the functional group containing phosphorus (phosphates vs. phosphites) may lead to chemistry-based differences throughout this subclass despite structural similarities amongst the members. One member of this subclass was found to have a halogenated heterocycle group as a substituent instead.

Table 5-1 lists 42 individual chemicals in the PHOP subclass. Two pairs of chemicals may refer to the same substance (CAS RN 1067-98-7 and 26248-87-3; and CAS RN 115-96-8 and 29716-44-7). In these cases, staff will consider data under either CAS RN for analyses concerning the substance.

Table 5-1. List of Chemicals in PHOP Subclass

	CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
1	1047637-37-5	2,2-Bis(chloromethyl)-1,3-propanediyl tetrakis(1-chloro-2-propanyl) bis(phosphate)	BCMP-BCMEP	CC(CCl)OP(=O)(OCC(COP(=O)(OC(C)CCl)OC(C)CCl)(CCl)CCl)OC(C)CCl
2	1067-98-7	Tris(3-chloropropyl)phosphate	NA	C(COP(=O)(OCCCCl)OCCCCl)CCl
3	115-96-8	Tris(2-chloroethyl)phosphate	TCEP	C(CCl)OP(=O)(OCCCl)OCCCl
4	115-98-0	Bis(2-chloroethyl) vinylphosphonate	NA	C=CP(=O)(OCCCl)OCCCl
5	125997-20-8	Phosphoric acid, mixed 3-bromo-2,2-dimethylpropyl and 2-bromoethyl and 2-chloroethyl esters	NA	CC(C)(COP(=O)(OCCCl)OCCBr)CBr
6	126-72-7	Tris(2,3-dibromopropyl)phosphate	TDBPP	C(C(CBr)Br)OP(=O)(OCC(CBr)Br)OCC(CBr)Br
7	13674-84-5	Tris(2-chloroisopropyl)phosphate	TCIPP, TCPP	CC(CCl)OP(=O)(OC(C)CCl)OC(C)CCl
8	13674-87-8	Tris(1,3-dichloro-2-propyl)phosphate	TDCIPP, TDCPP	C(C(CCl)OP(=O)(OC(CCl)CCl)OC(CCl)CCl)Cl
9	1373346-90-7	dimethyl {[(4,6-dichloro-1,3,5-triazin-2-yl)oxy]methyl}phosphonate	NA	COP(=O)(COC1=NC(=NC(=N1)Cl)Cl)OC
10	140-08-9	Tris(2-chloroethyl)phosphite	NA	C(CCl)OP(OCCCl)OCCCl
11	19186-97-1	Tris(tribromoneopentyl)phosphate	TTBNPP	C(C(CBr)(CBr)CBr)OP(=O)(OCC(CBr)(CBr)CBr)OCC(CBr)(CBr)CBr
12	26248-87-3	Tris(chloropropyl)phosphate	NA	C(COP(=O)(OCCCCl)OCCCCl)CCl
13	26604-51-3	Tris(dichloropropyl)phosphate	NA	CC(C(OP(=O)(OCCC(Cl)Cl)OCC(CCl)Cl)Cl)Cl
14	27568-90-7	Ethanol, 2-bromo, phosphate (3:1)	NA	C(CBr)OP(=O)(OCCBr)OCCBr
15	2788-11-6	Tris(2,4-dibromophenyl)phosphate	NA	C1=CC(=C(C=C1Br)Br)OP(=O)(OC2=C(C=C(C=C2)Br)Br)OC3=C(C=C(C=C3)Br)Br
16	29716-44-7	Tris(chloroethyl)phosphate	NA	C(CCl)OP(=O)(OCCCl)OCCCl
17	33125-86-9	Phosphoric acid, 1,2-ethanediyl tetrakis(2-chloroethyl) ester	NA	C(COP(=O)(OCCCl)OCCCl)OP(=O)(OCCCl)OCCCl
18	34432-82-1	Bis(2,3-dibromopropyl) hydrogen phosphate--ammonia (1/1)	NA	C(C(CBr)Br)OP(=O)(O)OCC(CBr)Br.N
19	34621-99-3	Tetrakis(1-chloropropan-2-yl) ethane-1,2-diyl bis(phosphate)	NA	CC(CCl)OP(=O)(OCCOP(=O)(OC(C)CCl)OC(C)CCl)OC(C)CCl

	CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
20	35656-01-0	Tris(2bromo4methylphenyl)phosphate	NA	CC1=CC(=C(C=C1)OP(=O)(OC2=C(C=C(C=C2)C)Br)OC3=C(C=C(C=C3)C)Br)Br
21	36711-31-6	Bis(2,3-dibromopropyl)phosphate, magnesium salt	NA	C(C(CBr)Br)OP(=O)([O-])OCC(CBr)Br.C(C(CBr)Br)OP(=O)([O-])OCC(CBr)Br.[Mg+2]
22	38051-10-4	Phosphoric acid, 2,2-bis(chloromethyl)-1,3-propanediyl tetrakis(2-chloroethyl) ester	BCMP-BCEP, V6	C(CCl)OP(=O)(OCCCl)OCC(COP(=O)(OCCCl)OCCCl)(CCl)CCl
23	40120-74-9	Tris(1,3-dichloropropyl)phosphate	NA	C(CCl)C(OP(=O)(OC(CCCl)Cl)OC(CCCl)Cl)Cl
24	4351-70-6	Phosphonic acid, P-[1-[[(2-chloroethoxy)(2-chloroethyl)phosphinyl]oxy]ethyl]-, 1-[bis(2-chloroethoxy)phosphinyl]ethyl 2-chloroethyl ester	NA	CC(OP(=O)(C(C)OP(=O)(OCCCl)OCCCl)OCCCl)OCCCl)P(=O)(OCCCl)OCCCl
25	49690-63-3	Tris(dibromophenyl)phosphate	NA	C1=CC(=C(C=C1Br)Br)OP(=O)(OC2=C(C=C(C=C2)Br)Br)OC3=C(C=C(C=C3)Br)Br
26	5324-12-9	2,3-Dibromopropylphosphate	NA	C(C(CBr)Br)OP(=O)(O)O
27	53461-82-8	Diethylene glycol bis[bis(2-chloroethyl)phosphate]	NA	C(COP(=O)(OCCCl)OCCCl)OCCOP(=O)(OCCCl)OCCCl
28	5412-25-9	Bis(2,3-dibromopropyl) hydrogen phosphate	NA	C(C(CBr)Br)OP(=O)(O)OCC(CBr)Br
29	61090-89-9	2,4,8,10-Tetraoxa-3,9-diphosphaspiro[5.5]undecane, 3,9-bis[3-bromo-2,2-bis(bromomethyl)propoxy]-, 3,9-dioxide	NA	C1C2(COP(=O)(O1)OCC(CBr)(CBr)CBr)COP(=O)(OC2)OCC(CBr)(CBr)CBr
30	6145-73-9	Tris(2-chloropropyl)phosphate	NA	CC(COP(=O)(OCC(C)Cl)OCC(C)Cl)Cl
31	6294-34-4	Bis(2-chloroethyl) 2-chloroethylphosphonate	NA	C(CCl)OP(=O)(CCCl)OCCCl
32	64864-08-0	Sodium bis(2,3-dibromopropyl)phosphate	NA	C(C(CBr)Br)OP(=O)([O-])OCC(CBr)Br.[Na+]
33	66108-37-0	2,2-Bis(bromomethyl)-3-chloropropyl bis[2-chloro-1-(chloromethyl)ethyl]phosphate	NA	C(C(CCl)OP(=O)(OCC(CCl)(CBr)CBr)OC(CCl)CCl)Cl
34	66519-18-4	potassium bis(2,3-dibromopropyl)phosphate	NA	C(C(CBr)Br)OP(=O)([O-])OCC(CBr)Br.[K+]
35	6749-73-1	Tris(1,3-dichloropropan-2-yl)phosphite	NA	C(C(CCl)OP(OC(CCl)CCl)OC(CCl)CCl)Cl

	CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
36	7046-64-2	Tris(2,4,6-tribromophenyl)phosphate	NA	C1=C(C=C(C(=C1Br)OP(=O)(OC2=C(C=C(C=C2Br)Br)Br)OC3=C(C=C(C=C3Br)Br)Br)Br)Br
37	72236-72-7	Bis(1,3-dichloropropan-2-yl) hydrogen phosphate	NA	C(C(CCl)OP(=O)(O)OC(CCl)CCl)Cl
38	76025-08-6	Bis(2-chloro-1-methylethyl) 2-chloropropyl phosphate	NA	CC(COP(=O)(OC(C)CCl)OC(C)CCl)Cl
39	76649-15-5	(2-Chloro-1-methylethyl) bis(2-chloropropyl)phosphate	NA	CC(COP(=O)(OCC(C)Cl)OC(C)CCl)Cl
40	78-43-3	Tris(2,3-dichloropropyl)phosphate	TDCPP	C(C(CCl)Cl)OP(=O)(OCC(CCl)Cl)OCC(CCl)Cl
41	84282-27-9	2-Bromoethyl 5-bromopentyl 2-chloroethyl phosphate	NA	C(CCOP(=O)(OCCCl)OCCBr)CCBr
42	98923-48-9	4-Bromo-2-chlorobutyl 3-bromo-2,2-dimethylpropyl phosphate	NA	CC(C)(COP(=O)(OCCCl)OCCBr)CBr

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

5.1.1. Physicochemical Property Summaries

The information collected to date led CPSC staff to find that experimental physicochemical data on PHOP chemicals are limited and can vary considerably, by orders of magnitude, for some class members. Eleven PHOP subclass members have experimental data and 38 PHOP members have predicted data. Well-studied chemicals in this subclass include tris(2-chloroethyl)phosphate (TCEP, CAS RN 115-96-8), tris(2-chloroisopropyl)phosphate (TClPP, CAS RN 13674-84-5) and tris(1,3-dichloro-2-propyl)phosphate (TDClPP, CAS RN 13674-87-8). From this data set, studied PHOPs have boiling points ranging from 130°C to 400°C, and vapor pressures from 7.5×10^{-6} to 2.31×10^{-1} mm Hg. Data show water solubility values ranging from 2.00×10^{-8} to 2.62×10^{-2} mol/L. The octanol/water partition coefficient (K_{ow}) values, which are commonly expressed as log Kow, range from 0.58 to 4.8. A detailed list of experimental and predicted physicochemical values are located in the supplemental file for chemical descriptors and physicochemical properties (Supplemental File: Chemical Descriptors and Physicochemical Properties for PHOP Class and Analogs) (see Appendix: Supporting Files).

5.2. Market and Use Summary for PHOPs

The OFR Market and Use Report, completed in March 2022, includes 42 PHOP chemicals.

- Forty PHOP chemicals had market and use information and two chemicals had no market and use information.
- According to EPA data, 11 PHOP chemicals were identified to be on the EPA TSCA chemical substance (active) inventory, 12 PHOP chemicals were identified on the TSCA (inactive) inventory, four were on the CDR, and one was on the TRI program list.
- Five PHOP chemicals were identified in the Interstate Chemicals Clearinghouse (IC2) HPCDS.
- Twelve PHOP chemicals were identified in the targeted literature search.
- Twenty-nine PHOP chemicals had patent data.

5.2.1. PHOPs 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 40 PHOPs that are known to be or have been used in commerce, according to data available from these sources.

The two PHOP chemicals that are not known to be used in commerce are: 4-bromo-2-chlorobutyl 3-bromo-2,2-dimethylpropyl phosphate (CAS RN 98923-48-9) and dimethyl {[(4,6-dichloro-1,3,5-triazin-2-yl)oxy]methyl}phosphonate (CAS RN 1373346-90-7).

Among the 40 PHOP chemicals used in commerce, 23 are found on the TSCA inventory. Eleven of these chemicals are on the TSCA active inventory and 12 PHOPs are on the TSCA inactive inventory. In Table 5-2, PHOP chemicals found on the TSCA inventory are identified as “Active” or “Inactive,” accordingly.

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

[11] EU REACH = European Union Registration, Evaluation, Authorisation, and Restriction of Chemicals; INSQ = Inventario Nacional de Sustancias Químicas; CSCL= Chemical Substances Control Law; IECSC = Inventory of Existing Chemical Substances Produced or Imported in China.

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

Twenty-nine PHOP 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. PHOP Chemicals Used in Commerce

CAS RN	Chemical Name	TSCA	International Inventories	Literature Cites	Patents
1047637-37-5	2,2-Bis(chloromethyl)-1,3-propanediyl tetrakis(1-chloro-2-propanyl) bis(phosphate)	Not found	1	0	0
1067-98-7	Tris(3-chloropropyl)phosphate	Not found	Not found	0	4,255
115-96-8	Tris(2-chloroethyl)phosphate	Active	4	27	19,141
115-98-0	Bis(2-chloroethyl) vinylphosphonate	Inactive	1	1	1,261
125997-20-8	Phosphoric acid, mixed 3-bromo-2,2-dimethylpropyl and 2-bromoethyl and 2-chloroethyl esters	Inactive	1	0	7
126-72-7	Tris(2,3-dibromopropyl)phosphate	Active	3	8	10,811
13674-84-5	Tris(2-chloroisopropyl)phosphate	Active	4	24	1,751
13674-87-8	Tris(1,3-dichloro-2-propyl)phosphate	Active	5	44	5,202
140-08-9	Tris(2-chloroethyl)phosphite	Active	3		1,562
19186-97-1	Tris(tribromoneopentyl)phosphate	Active	4	5	No CID
26248-87-3	Tris(chloropropyl)phosphate	Not found	1	2	4,255
26604-51-3	Tris(dichloropropyl)phosphate	Not found	1	1	0
27568-90-7	Ethanol, 2-bromo-, phosphate (3:1)	Not found	Not found	0	129
2788-11-6	Tris(2,4-dibromophenyl)phosphate	Not found	Not found	0	405
29716-44-7	Tris(chloroethyl)phosphate	Not found	Not found	0	19,141
33125-86-9	Phosphoric acid, 1,2-ethanediyl tetrakis(2-chloroethyl) ester	Inactive	1	0	2,444

[12] For additional detail on the methodology used for the targeted literature search, see Section 4.3.1, Targeted Literature Search, in this scope document.

CAS RN	Chemical Name	TSCA	International Inventories	Literature Cites	Patents
34432-82-1	Bis(2,3-dibromopropyl) hydrogen phosphate--ammonia (1/1)	Inactive	1	0	0
34621-99-3	Tetrakis(1-chloropropan-2-yl) ethane-1,2-diyl bis(phosphate)	Inactive	Not found	0	0
35656-01-0	Tris(2-bromo-4-methylphenyl)phosphate	Not found	Not found	0	162
36711-31-6	Bis(2,3-dibromopropyl)phosphate, magnesium salt	Not found	1	0	0
38051-10-4	Phosphoric acid, 2,2-bis(chloromethyl)-1,3-propanediyl tetrakis(2-chloroethyl) ester	Active	4	9	360
40120-74-9	Tris(1,3-dichloropropyl)phosphate	Not found	1		3,094
4351-70-6	Phosphonic acid, P-[1-[[(2-chloroethoxy)(2-chloroethyl)phosphinyl]oxy]ethyl]-, 1-[bis(2-chloroethoxy)phosphinyl]ethyl 2-chloroethyl ester	Inactive	Not found	0	165
49690-63-3	Tris(dibromophenyl)phosphate	Not found	1	0	No CID
5324-12-9	2,3-Dibromopropylphosphate	Not found	1	0	192
53461-82-8	Diethylene glycol bis[bis(2-chloroethyl)phosphate]	Inactive	1	0	0
5412-25-9	Bis(2,3-dibromopropyl) hydrogen phosphate	Inactive	1	1	435
61090-89-9	2,4,8,10-Tetraoxa-3,9-diphosphaspiro[5.5]undecane, 3,9-bis[3-bromo-2,2-bis(bromomethyl)propoxy]-, 3,9-dioxide	Inactive	Not found	0	0
6145-73-9	Tris(2-chloropropyl)phosphate	Active	2	2	7,335
6294-34-4	Bis(2-chloroethyl) 2-chloroethylphosphonate	Active	3	0	448
64864-08-0	Sodium bis(2,3-dibromopropyl)phosphate	Not found	1	0	0
66108-37-0	2,2-Bis(bromomethyl)-3-chloropropyl bis[2-chloro-1-(chloromethyl)ethyl]phosphate	Inactive	Not found	0	9
66519-18-4	potassium bis(2,3-dibromopropyl) phosphate	Not found	1	0	0

CAS RN	Chemical Name	TSCA	International Inventories	Literature Cites	Patents
6749-73-1	Tris(1,3-dichloropropan-2-yl)phosphite	Inactive	1	0	4
7046-64-2	Tris(2,4,6-tribromophenyl)phosphate	Not found	2	0	508
72236-72-7	Bis(1,3-dichloropropan-2-yl) hydrogen phosphate	Not found	1	2	1
76025-08-6	Bis(2-chloro-1-methylethyl) 2-chloropropyl phosphate	Active	3	0	10
76649-15-5	(2-Chloro-1-methylethyl) bis(2-chloropropyl) phosphate	Active	3	0	9
78-43-3	Tris(2,3-dichloropropyl)phosphate	Inactive	2	0	6,276
84282-27-9	2-Bromoethyl 5-bromopentyl 2-chloroethyl phosphate	Not found	Not found	0	4

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

5.2.2. PHOPs Used in Consumer Products

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

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

- Furniture foam (6.6%)
- Toys, specifically second-hand toys (median 5%)
- Baby chairs and carriers (up to 4.4%)
- Curtains and wallpaper (<0.1%)
- Textiles/foam and other baby products (<0.1%)

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

CAS RN 115-96-8: polyurethane foam (PUF) for upholstered furniture and baby products, soft plastic and rubber toys, baby nap mats, portable cribs, nursing pillows, baby carriers, car seats,

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

sleeping wedges, changing table pads, and nursing bath slings. It has been used in polyvinyl chloride (PVC) and roofing insulation, in coatings and adhesives (including cellulose and polyester resins), and in textiles (including back coatings for carpets and in curtains). It has also been used in some electronics, such as TV casings.

CAS RN 126-72-7: baby textiles, soft non-PVC toys, baby mattresses, and diaper-changing mats.

CAS RN 13674-84-5: durable infant or toddler products, toys, childcare articles, car seats, mattresses and mattress pads, electronic devices, resins and latexes, spray polyurethane foam insulation (spray foam), and wallpaper. It has also been used in building insulation and refrigerator casings, isocyanurate PUF (usually rigid), PVC, ethylene vinyl acetate and phenolics, and epoxy resins.

CAS RN 13674-87-8: PUF (furniture and automotive), camping tents and other textiles (including curtains), children's car seats, strollers, sleeping mattresses and nursing pillows, gymnasium foam blocks, carpet padding, plastics, resins, textile coatings, rubber, wallpaper, and electronics (LCD TV components, laptop components).

CAS RN 19186-97-1: polypropylene products, such as carpets and stadium seats, and in curtains. The chemical is “recommended” for polypropylene, high-impact polystyrene, acrylonitrile butadiene styrene, extruded polystyrene foam, and polymer alloys, and in adhesives and fibers.

HPCDS. Using the HPCDS reporting tool, private industry reports the use of chemicals of concern in products intended for use by children that are sold in select states.[14] From 2012 to 2020, 1,093 reports were submitted to HPCDS identifying the use of OFR chemicals from seven subclasses in children’s products sold in two U.S. states, Washington and Oregon. Twenty-six percent, or 282 reports, documented the use of PHOP chemicals in children’s products, the most of any OFR subclass identified.

Table 5-3 shows the five PHOP chemicals reported in HPCDS to be used in children’s products. Of the 282 reported uses of PHOPs in children’s products, the majority (163) were for use as a chemical flame retardant. Of the 282 reported uses of PHOPs in children’s products, most chemicals were reportedly used in trace amounts, although 33 reports identified the use of PHOPs in children’s products in concentrations greater than 1,000 ppm (0.1%), a threshold CPSC staff considers above the level of contaminant.[15] There were 16 reported uses of PHOPs

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

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

in concentrations greater than 0.1% that were expressly for use as a chemical flame retardant in a children's product.

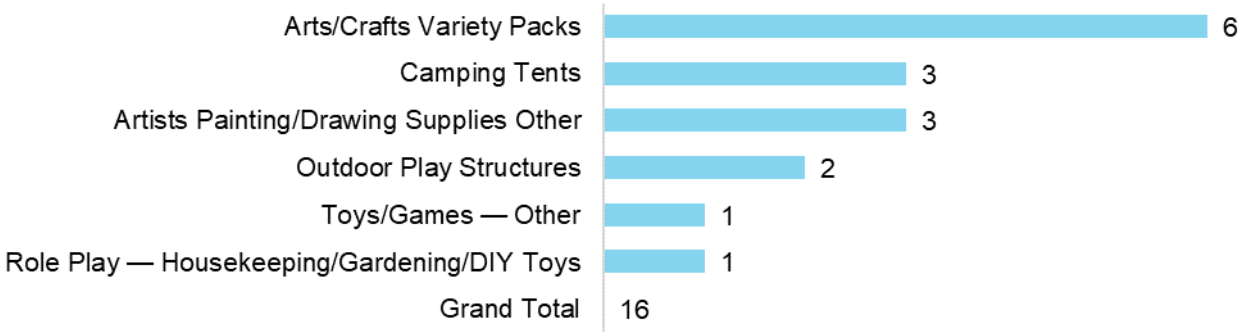
Table 5-3. Number of Children's Products with Reported Use as Flame Retardants for Select PHOP Chemicals

PHOPs	Total Report Count	Flame Retardant Use	Concentration >0.1%	Concentration >0.1% + FR Use
115-96-8	135	73	5	1
126-72-7	1	1	0	0
13674-84-5	35	18	16	12
13674-87-8	105	68	11	3
38051-10-4	6	3	1	0
Total	**282**	**163**	**33**	**16**

Source: HPCDS, Interstate Chemicals Clearinghouse.

As shown in Figure 5-1, the 16 reported applications for which PHOPs are used as chemical flame retardants (in concentrations greater than 0.1%) were children's arts and crafts variety packs, art painting and drawing supplies, camping tents, outdoor play structures, role play housekeeping, gardening, do-it-yourself toys, and other toys and games. (See Exhibit 3-28 in the Market and Use Report, Volume 1.)

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



Source: HPCDS, Interstate Chemicals Clearinghouse.

Among children's products identified to contain PHOP 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 PHOP 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)
13674-84-5	Tris (2-chloroisopropyl)phosphate	X	X
13674-87-8	Tris (1,3-dichloro-2propyl)phosphate	X	X
115-96-8	Tris (2-chloroethyl)phosphate	Not found	X

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

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

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

Table 5-5. PHOP Chemicals Included in SCIP Database

CAS RN	Substance Name	EC No.	Number of Search Results
115-96-8	Tris (2-chloroethyl)phosphate	204-118-5	20,396

As of June 2023, there were 20,396 search results for tris (2-chloroethyl) phosphate (CAS RN 115-96-8) in the SCIP database. Articles that contain this candidate list substance can be found in over 50 article categories that can be used to help identify articles based on function and use. According to SCIP data, tris (2-chloroethyl) phosphate can be found in vehicles, machinery and appliances, optical instruments, and plastic and rubber articles. 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, PHOP chemicals have been used in a variety of product use categories for many years (see Table 5-6). This table both commercial

and consumer product uses of PHOP chemicals because CPSC needs to know the range of product uses for these chemicals during the scoping phase.[16]

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 PHOP chemicals in the three reporting periods.[17] 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 PHOP chemicals are in building and construction materials, other products not identified, foam seating and bedding products, rubber and plastic products, and in adhesives and sealants, although PHOPs 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 PHOP Chemicals

Product Use Category	2006	2012	2016	Total
Building/construction materials not covered elsewhere	NR	10	11	**21**
Product description, not identified	3	2	6	**11**
Foam seating and bedding products	NR	4	4	**8**
Rubber and plastic products	4	1	2	**7**
Adhesives and sealants	NR	1	2	**3**
Electrical and electronic products	NR	1	1	**2**
Fabric, textile, and leather products not covered elsewhere	NR	1	1	**2**
Building/construction materials—wood and engineered wood products	NR	NR	1	**1**
Insulating foam	NR	NR	1	**1**
Paints and coatings	NR	1	NR	**1**
Grand Total	**7**	**21**	**29**	**57**

Notes: Data listed as "Product description not identified" may be interpreted as one of any of the other product categories reported for PHOPs, 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

[16] 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.
[17] 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.

in children's products.[18] In 2006, the use of PHOP chemicals in children's products was considered by reporting firms to be confidential business information (CBI) and the product category use of PHOP chemicals was also considered CBI. In 2012, the use of PHOP chemicals in children's products was considered by reporting firms to be not known or reasonably ascertainable (NKRA) for the following product category uses: building/construction materials; electrical and electronic products; fabric, textile, and leather products; foam sealing and bedding products; and paints and coatings. In 2016, the use of PHOP chemicals in children's products was considered by reporting firms to be NKRA for these same product category uses, except for paints and coatings.

5.2.3. Regulatory History and Trends for PHOPs

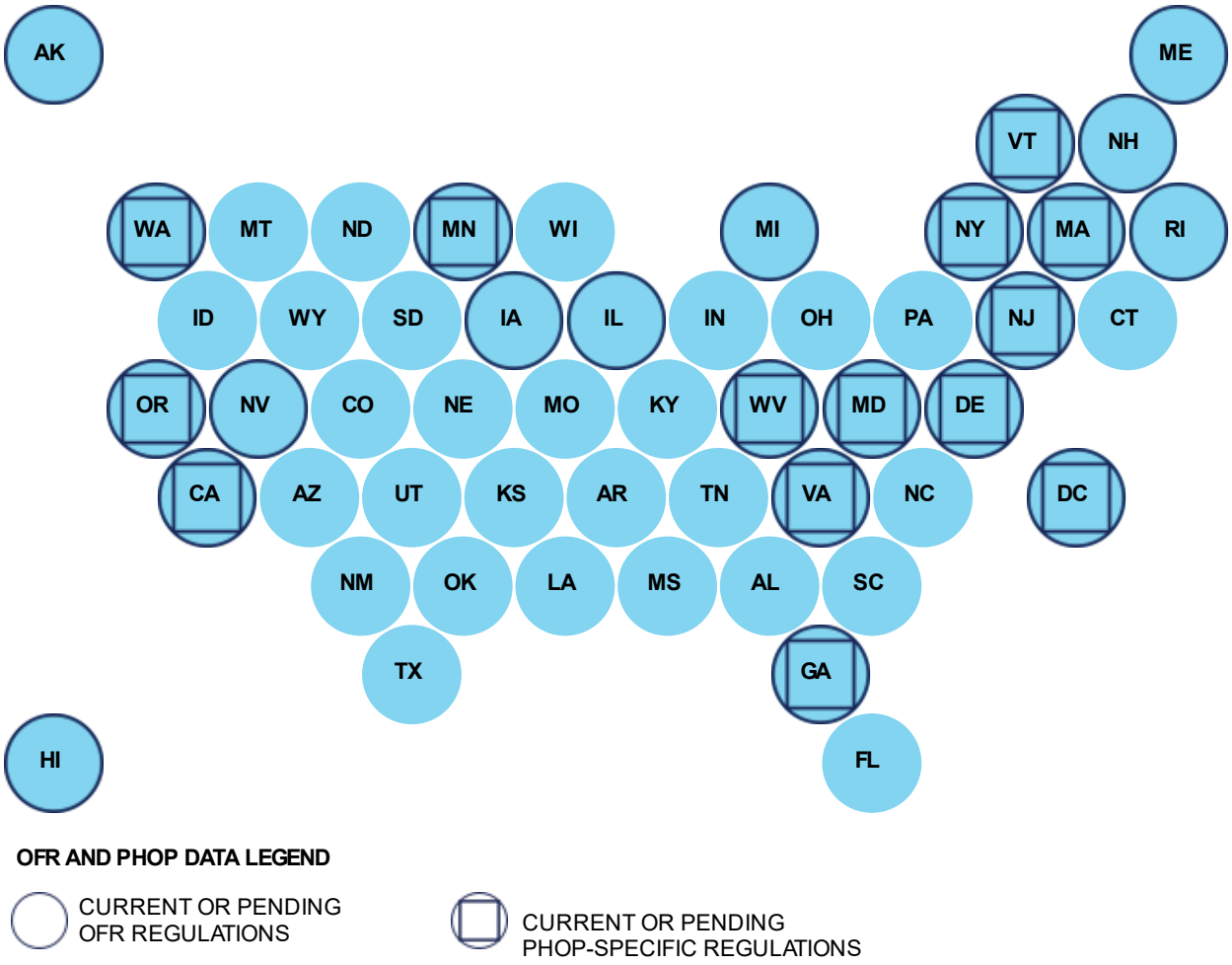
OFRs have received considerable regulatory attention from governmental jurisdictions in the United States and around the world; however, the scope and applicability of these regulatory actions varies significantly. This section discusses legislative action taken in the United States at the state level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

The Market and Use Report provides greater detail of legislative action taken in the United States, as well as action taken by other nations. Volume 2, Appendix R of the Market and Use Report provides detailed fact sheets describing specific pieces of legislation enacted or under consideration since 1986 in 21 U.S. states and the District of Columbia, at the U.S. federal level, and by Canada, the EU, and Japan.[19]

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, 10 states and the District of Columbia regulate the use of PHOPs specifically. An additional six states have legislation pending that would regulate the use of OFRs or PHOPs or both. In the map below (Figure 5-2), states that regulate OFRs or have pending regulations are shown with circles, and states that regulate PHOPs specifically or have pending PHOP-specific regulations are shown with a square within the circle. For more information on the state regulation of OFRs and PHOPs, see Volume 2 of the Market and Use Report, Appendix R.

[18] 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.
[19] 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 PHOP 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.[20] The database counts indicate either the number of sources within the database (if available) or the number of entries in the database (if no information on source is available) after attempts were made to remove duplicates. The unit for PDF counts is the individual PDF file. Level 3B tagging was performed on a subset of 25 toxicity assessments, toxicity literature reviews, and risk assessments selected from Level 3 to identify even more specific information for the chemicals in these references. Note that most of the Level 3B data are from database data, and only a subset of the PDF data sources is tagged at Level 3B.

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

- PHOP members TCEP, TCIPP (also known as TCPP), and TDCIPP (also known as TDCPP) had the highest number of toxicity data sources in each category.
- PHOP members TCEP, TCIPP, and TDCIPP had the most representation across toxicity categories for database and PDF reviews.
- The *QSAR, Read-across, Analog* category (QSAR = quantitative structure activity relationships) had broad representation with 88% of PHOP members and 97% of analogs having at least one data source at Level 3 review and similar representation at Level 3B.

5.3.1. Summary of Level 2

The "Integrated" tab contains summed Level 2 toxicity data counts across PDF and database data.[21]

The literature survey identified integrated data sources (sum of databases and PDFs) for all 42 PHOP members and for 74 of 76 analogs. The PHOP members with the most data sources were TCEP, TDCIPP, TDBPP, and TCIPP. Table 5-7 summarizes how many PHOP members and analogs had different degrees of data source abundance.

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	
	PHOP Chemicals (n = 42)	Analog Chemicals (n = 76)
21+	4	0
6–20	10	1
1–5	28	73
0	0	2

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

5.3.2. Summary of Levels 3 and 3B

The "TOX_Integrated" tabs from each file contain Level 3 and Level 3B toxicity data counts across all toxicity databases and PDFs.[22] 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 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 PHOP 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						
	PHOP Chemicals (n = 42)						
	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+	6	1	3	11	36	4	6
6–20	7	2	8	2	6	4	7
1–5	7	4	25	2	0	11	4
0	22	35	6	27	0	23	25

[22] See evidence map file "PHOP Level 3 Evidence Maps 12.2.22, Tab: TOX Integrated" and "PHOP 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 20 PHOP members and four analogs at Level 3 review. Nineteen PHOP members and four analogs had data in the databases and PDFs at Level 3B review. The one PHOP with data at Level 3 but not 3B had data in a PDF that was not selected for extraction. 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:

- PHOP members TCEP, TCIPP, and TDCIPP had data sources in all subcategories.
- PHOP member TDBPP had data sources for all subcategories except Neurotoxicity and Endocrine Disruption.
- PHOP member BCMP-BCEP, BCMP-BCMEP, and TTBNPP had data sources for all subcategories except Neurotoxicity, Carcinogenicity, and Endocrine Disruption.
- Acute Toxicity and Mutagenicity/Genotoxicity were the subcategories with data sources for the most PHOP members.
- The data sources for the four analogs were all in the Acute Toxicity 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 PHOP Analogs (n = 76)						
	Animal Toxicity or Accepted Alternative	Human Toxicity	Human, Animal, or Modeled Toxicokinetics (ADME)	Experimental Mechanistic	QSAR, Read-Across, Analog	Qualitative Hazard Characterization	Quantitative Hazard Characterization
21+	0	0	0	0	23	0	0
6–20	2	0	0	1	4	0	2
1–5	2	1	23	1	47	4	2
0	72	75	53	74	2	72	72

Human Toxicity data sources were available for seven PHOP members and one analog at Level 3 review. Three PHOP members and no 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:

- PHOP member TDCIPP had the highest number of hits (32) with data sources in all subcategories except Irritation.
- PHOP member TCEP had data sources in all subcategories except Acute Toxicity.
- PHOP member TCIPP had data sources in all subcategories except Acute Toxicity and Irritation.

Human, Animal, or Modeled Toxicokinetics (ADME [absorption, distribution, metabolism, and excretion]*)* data sources were available for 36 PHOP members and 23 analogs at Level 3 review. Thirty-five PHOP members and 22 analogs had data 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 PHOP members or analogs under the subcategory Chemical- or Class-Specific PBPK Model.
- PHOP members TDCIPP, TCEP, and TCIPP had data sources in all subcategories except Chemical- or Class-Specific PBPK Model.
- The subcategory with the most data sources and for the most chemicals was Chemical- or Class-Specific QSAR for an ADME Parameter, with data sources identified for 35 PHOP members and 22 analogs.

Experimental Mechanistic data sources were available for 15 PHOP members and two analogs at Level 3 review. Eight PHOP members and no analogs had data in the databases and PDFs at Level 3B review.[23] 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.[24] CPSC staff observed the following:

- Four PHOP members had data sources in both subcategories. These were TCEP, TDBPP, TCIPP, and TDCIPP. Some of these hit counts were large, with hundreds or thousands of data sources per chemical per subcategory.
- The remaining four PHOP members with data sources in this category had hits only in the subcategory Study Makes Connection to MOA and Potential Health Effect. Two of these had large numbers of data sources (352 and 488, respectively).

QSAR, Read-Across, Analog data sources were available for all 42 PHOP members and 74 of 76 analogs at Level 3 review. All 42 PHOP members and 74 analogs had data 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:

- No data sources for PHOP 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 the majority of PHOP members per subcategory.
- All but two of the analogs had at least one data source for the Acute Toxicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental Toxicity, and Endocrine Disruption subcategories.

Qualitative Hazard Characterization data sources were available for 19 PHOP members and four analogs at Level 3 review. Fifteen PHOP members and four 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:

[23] 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.
[24] Many database sources could not be tagged for Level 3B because it was not clear whether a connection was made to MOA.

- PHOP members TCIPP, TDCIPP, and TCEP had data sources for each of the nine subcategories.
- PHOP member TDBPP had data sources in all subcategories except Endocrine Disruption.
- Including those mentioned above, 12 PHOP members and four analogs had data sources for Acute Toxicity.

Quantitative Hazard Characterization data sources were available for 17 PHOP members and four analogs at Level 3 review. Fifteen PHOP members and four 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:

- Of the 15 PHOP members and four analogs that had data sources at Level 3B review, all had hits for Acute Toxicity. PHOP members TCEP, TCIPP, and TDCIPP had the highest counts within this subcategory.
- PHOP member TCIPP had data sources available in all seven subcategories.

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.[25] 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. PHOP 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:

- PHOP members TCEP, TCIPP, and TDCIPP had the highest number of data sources in each category.
- PHOP members TCEP, TCIPP, and TDCIPP had the most representation across exposure categories for database and PDF reviews.

5.4.1. Summary of Level 2

The MMDB database and PDF searches identified exposure data sources for 31 of 42 PHOP members.[26] The PHOP members with the most data sources were TCEP, TDCIPP, TDBPP, and TCIPP. Table 5-10 summarizes how many PHOP members had different degrees of data source abundance. The PDFs provided more total data sources and covered more PHOP members than the database.

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

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
	PHOP Chemicals (n = 42)
21+	4
6–20	10
1–5	28
0	0

5.4.2. Summary of Levels 3 and 3B

The "EXP_Integrated" tabs from each file contains Level 3 and 3B exposure data counts.[27] The Level 3 integrated counts indicate the number of data sources per chemical from the MMDB database and identified PDFs. Level 3 counts were classified into six exposure data type categories. Integrated Level 3B counts report the sum of data sources from MMDB and a sample of 25 selected PDFs. At Level 3B, reviewers tagged the data sources to subcategories to provide additional details of specific data types. Table 5-11 summarizes how many PHOP 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					
	PHOP Chemicals (n = 42)					
	Environmental Monitoring	Biomonitoring/ Personal Monitoring	Source Characterization	Epidemiology – Population Group	Modeled Concentrations	Modeled Human Dose
21+	4	4	3	0	0	3
6–20	2	0	2	3	0	1
1–5	7	8	25	6	3	6
0	29	30	12	33	39	32

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

Environmental Monitoring data sources were available for 13 PHOP members at Level 3 review. Seven PHOP 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.

- PHOP members TDCIPP, TCEP, and TCIPP each had sources in all of the subcategories and high numbers of hits for the Indoor Dust and Outdoor Air subcategories.
- PHOP member tris(chloropropyl)phosphate had one source in each of the subcategories except Soil.
- PHOP members TDBPP and BCMP-BCEP had data sources for Indoor Dust only.
- PHOP member Bis(1,3-dichloropropan-2-yl) hydrogen phosphate had one data source each for Indoor Dust and Food/Dietary.

Biomonitoring/Personal Monitoring data sources were available for 12 PHOP members at Level 3 review. Six PHOP members had data 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).

- PHOP members TCEP, TDCIPP, and TCIPP had data sources in all of the subcategories.
- PHOP member tris(chloropropyl)phosphate had one data source each in the Breast Milk/Lipids and Skin/Dermal subcategories.
- PHOP member tris(2-chloropropyl) phosphate had two sources in the Blood/Serum subcategory.
- PHOP member Bis(1,3-dichloropropan-2-yl) hydrogen phosphate had 57 data sources for Urine.

Source Characterization data sources were available for 30 PHOP members at Level 3 review. Twenty-four PHOP 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.

- PHOP members TDCIPP, TCEP, and TCIPP each had data sources for all four subcategories.
- Twenty-two PHOP members, including the three noted above, had at least one data source for the subcategory Other Qualitative or Quantitative Description of Product Use or Class/Chemical.
- Three additional PHOP members each had one data source for the Product Testing: Content Only subcategory.

Environmental Epidemiology[28] data sources were available for nine PHOP members at Level 3 review. No data under this category were identified for any of the PHOP members in the Level

[28] 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.

3B review. The subcategories were Children; Adult, Non-Occupational; and Other, Specify (with Suggestions).

Modeled Concentrations data sources for three PHOP members were identified at Level 3 review. Level 3B reviews of the database and PDFs found one source in each of three subcategories (Indoor Concentration, Outdoor Concentration, and Dietary/Food) for TDCIPP.

Modeled Human Dose data sources were available for 10 PHOP members at Level 3 review. Five PHOP members had data in the database and PDFs at Level 3B review. The subcategories were Children; Adult, Non-occupational; and Other, Specify (with Suggestions).

- PHOP members TCEP, TCIPP, TDCIPP, and tris(chloropropyl)phosphate had data sources for the subcategories Children and Adult, Non-occupational.
- PHOP member Bis(1,3-dichloropropan-2-yl) hydrogen phosphate had one hit for Adult, Non-occupational only.
- The subcategory "Other, Specify (with Suggestions)" had no hits for any PHOP 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 sources.[29] No risk data were found in the databases. Ten PHOP members and no analogs had PDF data sources for risk at Level 2 review. Table 5-12 summarizes how many PHOP members had different degrees of data source abundance. TCEP, TDCIPP, and TCIPP 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
	PHOP Chemicals (n = 42)
21+	3
1–5	7
0	32

[29] 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.[30] 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 PHOP members and analogs had different degrees of Level 3 human health risk data source abundance.

Human Health Risk Assessment data were available for 10 PHOP members and no analogs at Level 3 review. Five PHOP members and no analogs had data in the 25 selected PDFs at Level 3B review. The subcategories used were Noncancer Risk and Cancer Risk, with 25 Noncancer Risk and nine Cancer Risk assessments identified. Staff noted the following observations:

- PHOP member TCEP had eight Noncancer Risk and four Cancer Risk data sources.
- PHOP member TDCIPP had nine Noncancer Risk and four Cancer Risk data sources.
- PHOP member TCIPP had six Noncancer Risk and one Cancer Risk data sources.
- PHOP members tris(chloropropyl)phosphate and BCMP-BCEP each had one Noncancer Risk data source.
- None of the PHOP analogs had risk assessment data sources.

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
	PHOP Chemicals (n = 42)
21+	3
1–5	7
0	32

5.6. Literature Survey Results: Key References

Among the literature survey results are several references from authoritative sources. These references include a toxicological profile by the Agency for Toxic Substances and Disease Registry, technical reports from the National Toxicology Program, EPA assessments and evaluations, Health Canada assessments, European Union risk assessment reports, International Agency for Research on Cancer evaluations, and Organisation for Economic Co-operation and Development assessments. Each of these references addressed one or more PHOPs. These reports included six specific PHOPs: TCEP, TDIPP, TCIPP, TDBPP, BCMP-BCEP, and tris(3-chloropropyl) phosphate. These six chemicals are among the PHOPs most frequently noted in the Market and Use Report as found in consumer products, as well as in the literature survey results generally. These reports suggest the existence of data about these

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

chemicals, including hazard and potential exposures, and may be useful references for CPSC staff evaluations of these and other PHOPs.

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 PHOP 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 PHOP subclass has sufficient data to proceed with risk assessment.**

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

CPSC staff concludes that the subclass includes 38 PHOP class members with some toxicity information and four class members with no toxicity information. Six PHOPs (no analogs) are potentially data rich, according to the literature survey evidence map, and could serve as anchor chemicals for read-across analysis. The evidence maps show that many PHOP 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 PHOP 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 40 PHOP class members with market-use information, 31 with some exposure information, and 11 class members with no exposure information. CPSC staff also concludes four PHOPs are potentially data rich chemicals and that a majority of chemicals have some data.

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

6.2. Next Steps for Class-Based Hazard Assessment

6.2.1. Analysis Plan

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

1. CPSC staff, in coordination with the Division of Translational Toxicology (DTT) at the National Institute of Environmental Health Sciences, is working on a comprehensive literature search. Available toxicity information from PHOP 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 PHOPs, data rich PHOP analogs, PHOPs with some toxicity information, and PHOPs 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][31]) from the comprehensive literature search.
3. CPSC staff will refine the NAS analog list and characterize analog substances for the PHOP class that are both chemically and toxicologically similar and have any amount of empirical toxicity information. Analog substances that are both data poor and not sufficiently similar to PHOP class members will be deprioritized. CPSC staff's initial survey shows that empirical toxicity data are available for four analogs and empirical toxicokinetic data are available for one analog.
4. CPSC staff will estimate major metabolites of PHOP 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 PHOP class members and analogs with available toxicity data can be used to read-across to PHOP 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 PHOP class are carcinogenicity, repeated dose toxicity, endocrine disruption, and developmental toxicity. Toxicity endpoints that are likely lower priority for the PHOP class are acute toxicity, irritation, sensitization, and reproductive toxicity.

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

6. CPSC staff will identify a smaller number of endpoint(s) and studies that are candidates for identifying points of departure (POD) and generating toxicity reference values for multiple PHOP 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 PHOP class members.
8. CPSC staff will explore the variability and uncertainty associated with dose-response values for PHOP 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 PHOPs.

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

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

NASEM included PHOPs as one of two case studies in its 2019 report. NASEM summarized the available data on developmental toxicity and developmental neurotoxicity (DNT) of PHOPs based on data for TDCPP (also known as TDCIPP), TCEP, TCPP (also known as TCIPP), and TDBPP. Some PHOPs or PHOP metabolites were associated with changes in sex or thyroid hormones in epidemiology studies, but several study limitations were noted. Inconsistent results were also noted for epidemiology studies for effects on cognition and memory. NASEM (2019) characterized the rodent data as negative for teratogenicity for all four PHOPs and negative for DNT for TDCPP and TCEP; data were not available for DNT for TCPP or TDBPP. Effects in zebrafish varied with the exposure period, but NASEM (2019) characterized TDCPP and TCEP as teratogenic in zebrafish, and all four PHOPs as being associated with DNT or altered locomotor activity.

PHOPs undergo rapid metabolism and have relatively short excretion half-lives, but ongoing exposure from a variety of sources can lead to ongoing internal body burden in humans (NASEM, 2019). In addition, some organophosphate diesters are metabolites of both PHOPs and of nonhalogenated organophosphates; there is therefore uncertainty regarding the chemical to which the individual was exposed (NASEM, 2019).

In its TSCA workplan for a cluster of three chlorinated phosphate ester FRs, EPA (2015) listed the endpoints of interest as cancer and effects on the kidney, liver, and neurological system; variability across studies was noted in effects on the thyroid, as well as with respect to

developmental and reproductive toxicity. Comparing results across class members is complicated by differences in study design.

Genotoxicity data are available for several PHOPs, including gene mutation assays in bacteria and mammalian cells, as well as in vitro and in vivo chromosome aberration assays. Results were primarily negative for the chlorinated PHOPs, with some positive in vitro gene mutation and chromosome aberration assays for TDCP (TDCIPP) and some scattered equivocal in vitro and in vivo results for TDCP and TCEP (ATSDR, 2012). Results for four more complex chlorinated and brominated PHOPs were also generally negative (ECHA, 2017, 2018, 2019, 2020). NASEM (2019) considered the data for genotoxicity of the PHOPs to be discordant, noting positive results for three brominated PHOPs that were not evaluated by ATSDR (2012).

Carcinogenicity studies in rodents have been conducted for four PHOPs or their metabolites, and results were recently published for a fifth PHOP (TCPP) (NTP, 2023). A wide range of tumor targets has been identified, without a clear pattern, although kidney tumors were noted in rodents exposed to TDCPP and TCEP and hepatocellular adenomas were noted for TDCPP and bis(2,3-dibromopropyl) hydrogen phosphate (NASEM, 2019).

Some information is available regarding PHOP MOA. Like other organophosphates, PHOPs are acetylcholinesterase inhibitors, but they are generally weak inhibitors, and the toxicological implications are uncertain. Neurological effects, including convulsions and hippocampal lesions have been reported in animal studies of high acute doses of TCEP (US EPA, 2015).

TDCIPP affected thyroid hormone levels in rats and zebrafish, with increased incidences of follicular cell hyperplasia in exposed rats (Hoffman et al., 2017). Alternative hypotheses for these effects include upregulation of clearance enzymes and antagonism of thyroid hormone receptor beta (TRβ) (Hoffman et al., 2017). In vitro studies (species not reported in the secondary reference) indicate that organophosphate esters (OPEs) act on a variety of signaling pathways, including the estrogen, androgen, glucocorticoid and pregnane X pathways (Hales and Robaire, 2020). It is unclear whether the PHOPs share this activity, although OPEs and PHOPs may share metabolites. The toxicological significance of any such interactions of the PHOPs is also unclear.

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 PHOP class members will be further summarized and integrated after this search is complete. After the search, staff will refine the list of data rich PHOPs, PHOPs with some exposure and use information, and PHOPs with no exposure and use information.

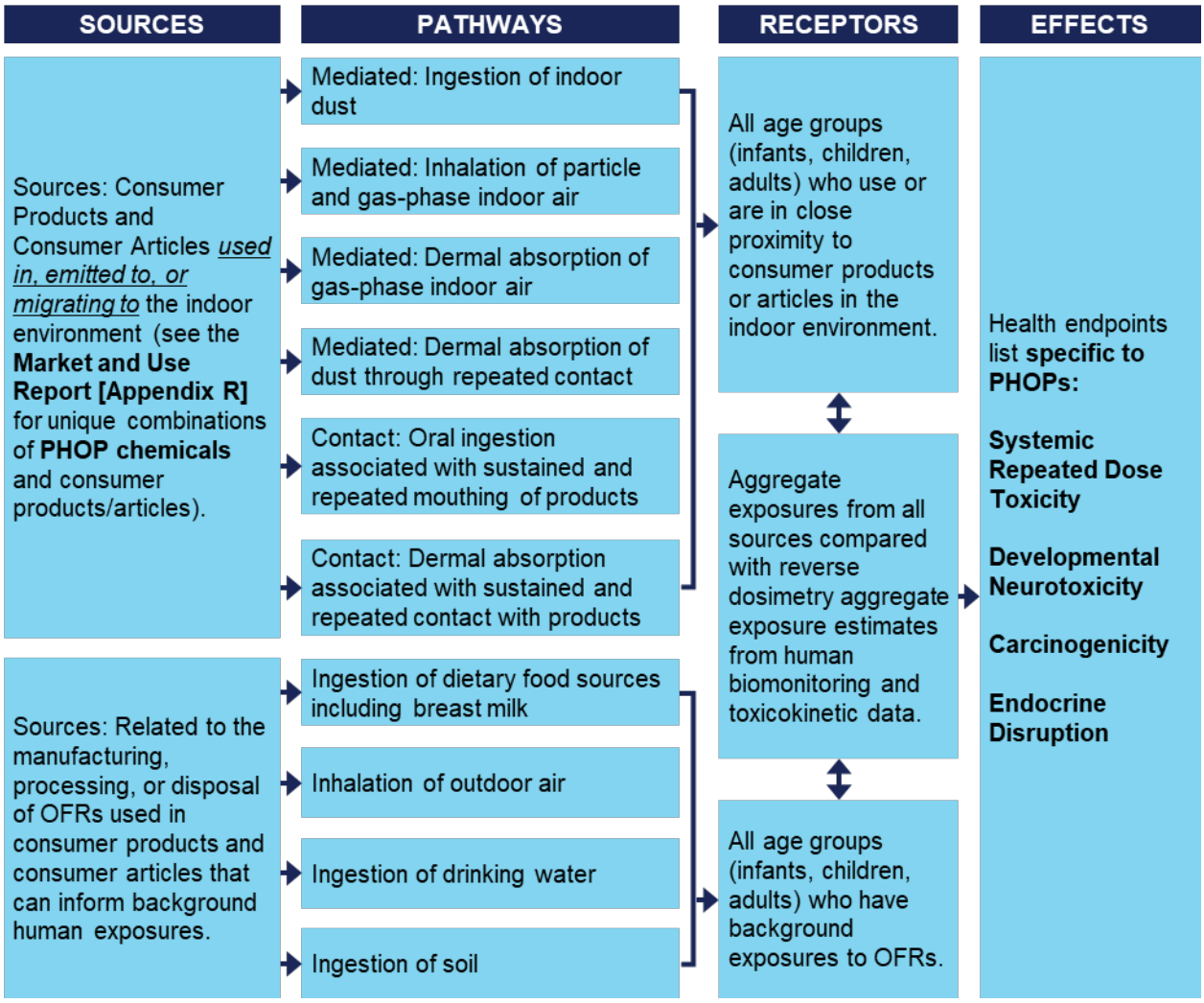
2. Using the market and use research, CPSC staff expects to compile a list of PHOP chemicals that have been or could be used in consumer products. While 40 of the 42 chemicals had some market-use information, 26 PHOP chemicals had more market and use information that could be used to inform analyses for PHOP chemicals with less information. CPSC staff will characterize uses for PHOPs 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 26 and 40 PHOP subclass members.
4. Exposure pathways with likely higher potential for PHOP 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 PHOP class members include inhalation of 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 30 chemicals in the class with source characterization data, 14 chemicals in the class with environmental monitoring data, and 13 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 PHOP 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 18 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 12 PHOP 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 PHOPs.

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 PHOP 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 PHOPs are listed.

Figure 6-1. PHOP Conceptual Exposure Model



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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 6-10.17.2022_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)

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Chemical Descriptors and Physicochemical Properties for PHOP Class and Analogs

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Literature Survey Results Supporting Files

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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.

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