



United States

Consumer Product Safety Commission

Organohalogen Flame Retardant Scope Document: Polyhalogenated Benzene Alicycle, Polyhalogenated Aliphatic Carboxylate, and Polyhalogenated Triazine Subclasses

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It has not been reviewed or approved by,
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Commission.*

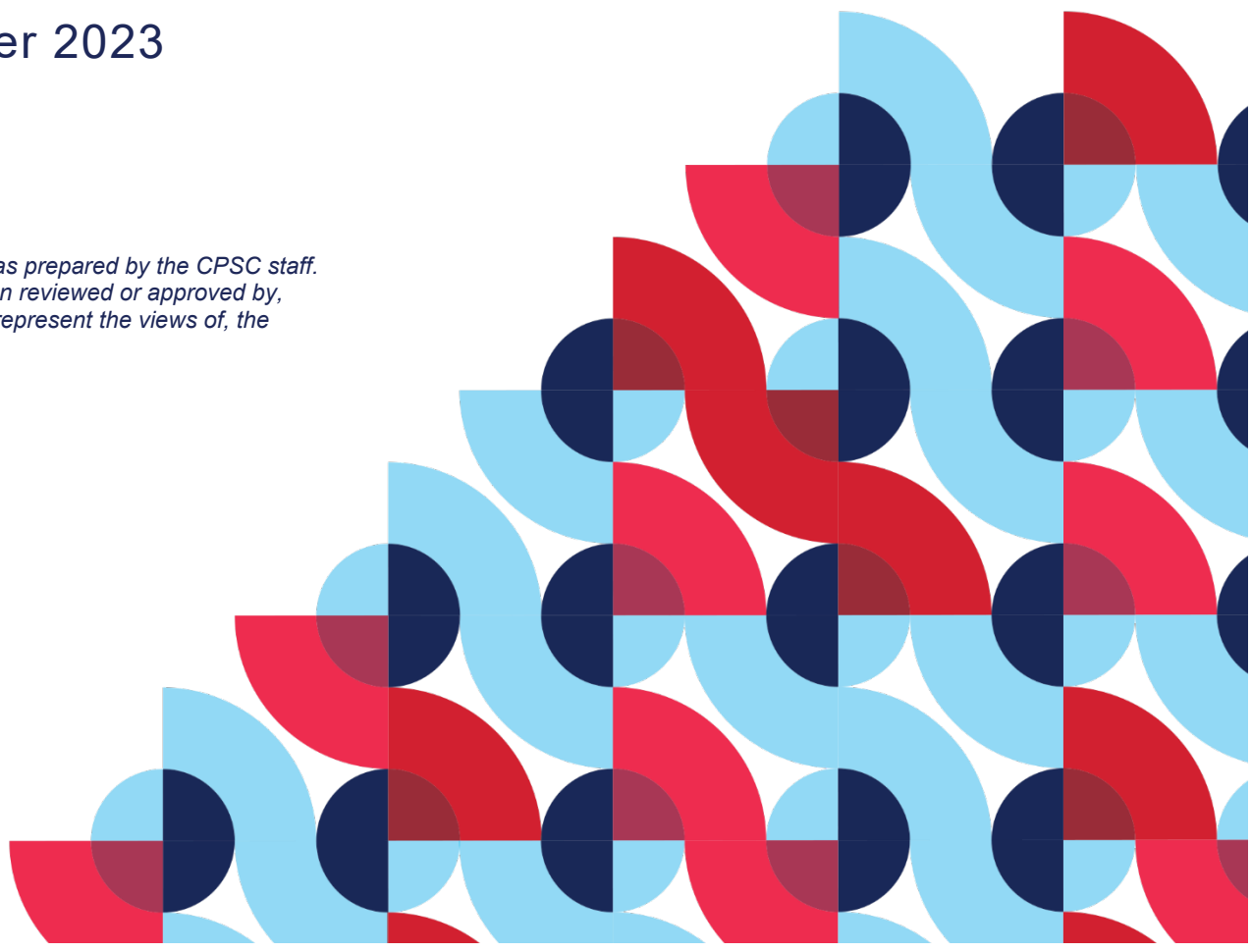


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1. Executive Summary

This scope document is for the polyhalogenated benzene alicycle (PHBA), polyhalogenated aliphatic carboxylate (PHACbx), and polyhalogenated triazine (PHT) subclasses of organohalogen flame retardants (OFRs). OFRs contain a carbon-halogen bond and are one of the main categories of flame retardants. Flame retardants (FR) are substances that alter the normal degradation or combustion processes of materials. They are incorporated into materials or used on surfaces to reduce or eliminate the tendency to ignite when exposed to heat or flame for a short period of time.

Informed by initial review of the market and use research, evidence maps, and availability of physicochemical data for the PHBA, PHACbx, and PHT subclasses and their analogs, as well as the Criteria for Scoping Determination described in this document, CPSC staff concludes, at the time of writing, that these subclasses do not have sufficient data to proceed with risk assessment. Next steps with respect to these three subclasses, as resources are available, involve monitoring to see if new data become available that would make it possible to proceed with a class-based assessment. Absent such data becoming available, staff would be required to propose lengthy and resource intensive contracted efforts to develop the data, which are not in current appropriations.

2. Introduction

This document contains the results of scoping efforts by Consumer Product Safety Commission (CPSC or the Commission) staff to characterize readily available information on the chemistry, uses, human toxicity, exposure, and human health risk of members of the polyhalogenated benzene alicycle (PHBA), polyhalogenated aliphatic carboxylate (PHACbx), and polyhalogenated triazine (PHT) subclasses of organohalogen flame retardants (OFRs). This document is one of many scope documents that CPSC staff produced to address each of 14 OFR chemical subclasses.

The primary question answered by this scope document 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 outlines the criteria for determining sufficiency for hazard assessments and exposure assessments, describes the data available, and provides the scoping determination for sufficiency to proceed. If the answer to the question above is yes, 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 have been prioritized for risk assessments.

If the answer is no, the scope document describes (i) CPSC staff's interpretation of available data through evidence maps and estimation approaches and (ii) key data gaps. These subclasses are 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, 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 hazard 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), at the direction of the Commission, CPSC staff developed a process for assessing the risks of OFRs in consumer products. A staff report to the Commission

¹ Project documents, including CPSC staff reports, contractor reports, and key references may be found on the [CPSC website](#) or [Docket No. CPSC-2015-0022](#).

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

4. Approach

4.1. Criteria for Scoping Determination

CPSC staff will determine whether a subclass has sufficient data, at this time, to proceed 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 (among 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.
 - 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 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 environmental monitoring, biomonitoring, product testing, or toxicokinetic study, 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 data likely support the ability to estimate a quantitative average daily dose for human exposure.
 - 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[®],² DTXSID,³

² 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.

³ 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.

and SMILES,⁴ 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.⁵ 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 of chemicals from the inventory or additions 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 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

⁴ Simplified molecular-input line-entry system (SMILES) describes the structure of a chemical in a way that can be used by a computer.

⁵ 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.⁶

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. It 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 Market and Use Report contains information describing national inventories and databases that were searched to determine whether OFRs were in commerce or present in consumer products. These three subclasses were included with all other subclasses when looking for this information. Other scope documents and the Market Use Report have more detailed information on methods.

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.

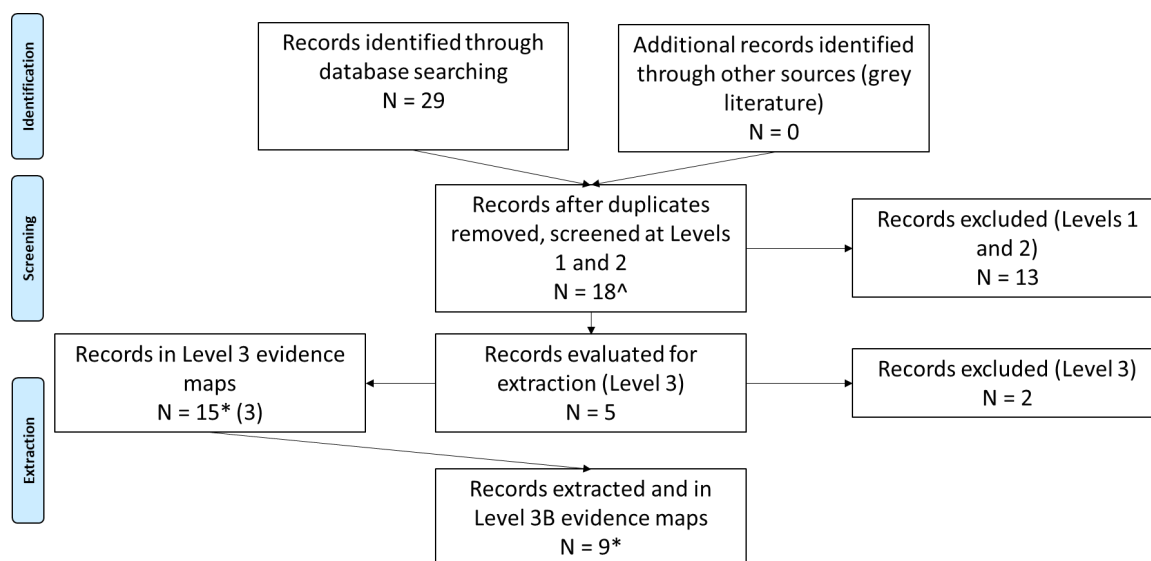
Detailed descriptions of the literature survey approach and process are found in the Literature Survey Guide and accompanying documentation. These documents were developed by University of Cincinnati (UC) Risk Science Center staff as part of work performed under a CPSC-sponsored contract (UC, 2022a; 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

⁶ For a list of data sources searched using Dialog/ProQuest, see Exhibit 3-32 of the Market and Use Report.

was relevant to the PECO statement.⁷ **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, Figure 4-2, and Figure 4-3 show the numbers of records initially identified and the number of records screened or extracted at each level.

Figure 4-1. Literature Flow Diagram (PHBA)



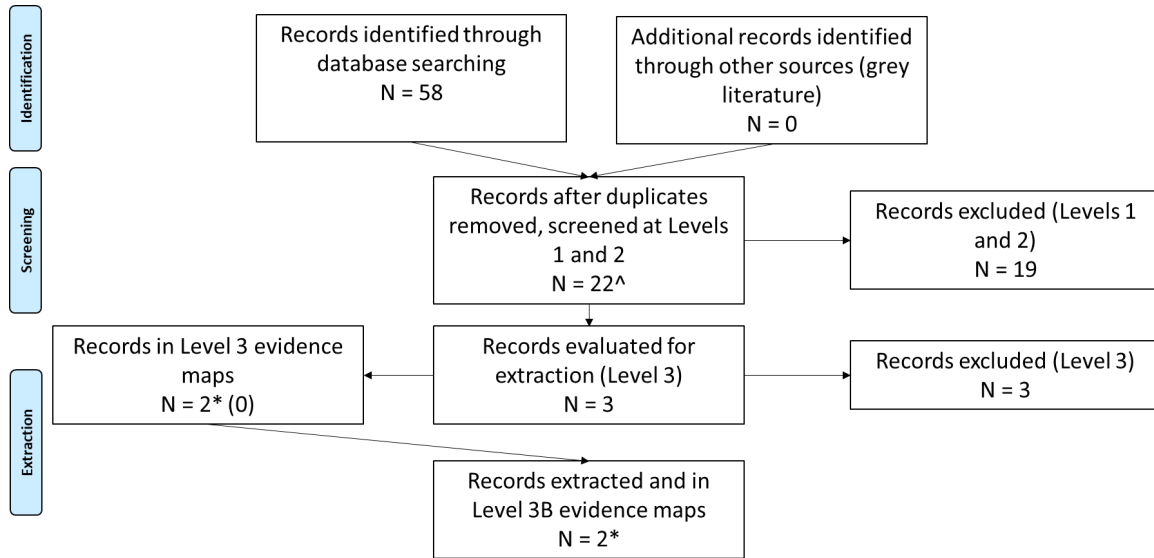
Notes:

[^]Removal of duplicates within the subclass and between this subclass and previous subclasses.

^{*}PHBA evidence maps contain additional references uploaded with other subclasses. Number in parentheses is the number of references identified by searching for the PHBA subclass only, excluding the references identified by searching for other subclasses.

⁷ 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 4-2. Literature Flow Diagram (PHACbx)

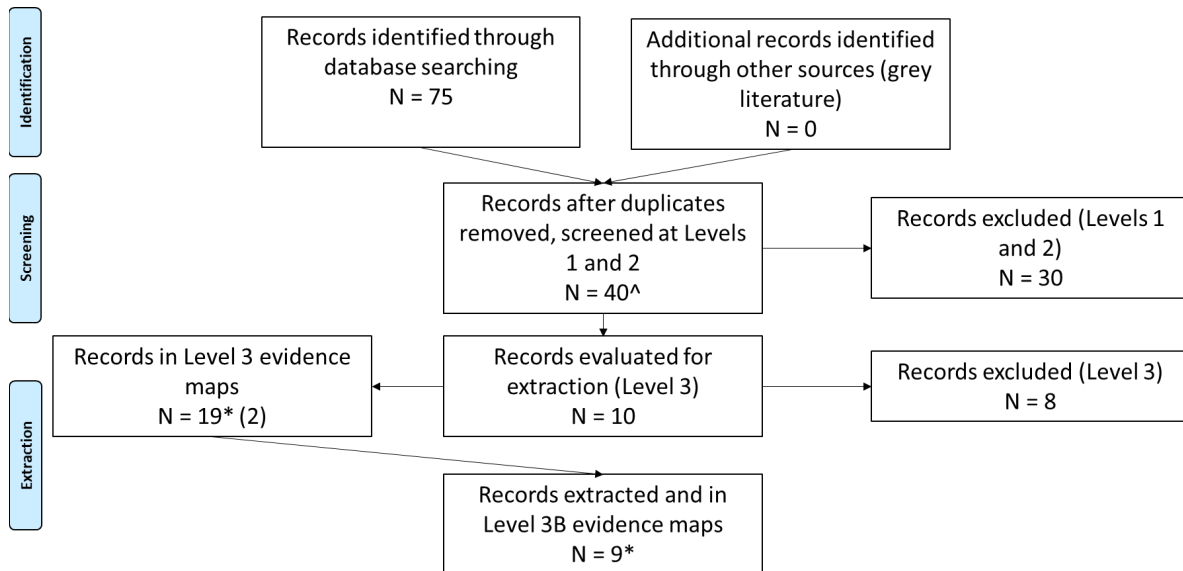


Notes:

^Removal of duplicates within the subclass and between this subclass and previous subclasses.

*PHACbx evidence maps contain additional references uploaded with other subclasses. Number in parentheses is the number of references identified by searching for the PHACbx subclass only, excluding the references identified by searching for other subclasses.

Figure 4-3. Literature Flow Diagram (PHT)



Notes:

^Removal of duplicates within the subclass and between this subclass and previous subclasses.

*PHT evidence maps contain additional references uploaded with other subclasses. Number in parentheses is the number of references identified by searching for the PHT subclass only, excluding the references identified by searching for other subclasses.

5. Scoping for Polyhalogenated Benzene Alicycles, Polyhalogenated Aliphatic Carboxylates, and Polyhalogenated Triazines

5.1.1 Polyhalogenated Benzene Alicycle Subclass Chemistry

The PHBA subclass consists of halogenated indene-derived polycyclic hydrocarbons. Members of this subclass all have a phenyl-functionalized indene derivative as a substructure. The phenyl group was also halogenated with between two to four halogen groups depending on the chemical. Table 5-1 lists the four individual chemicals in the PHBA subclass.

Table 5-1. List of Chemicals in Polyhalogenated Benzene Alicycle Subclass

CAS RN	Chemical Name	Abbreviation/ Synonyms	SMILES
1 1025956-65-3	2,4,5,6,7-Pentabromo-1,1,3-trimethyl-3-(2,4,6-tribromophenyl)-2,3-dihydro-1H-indene	NA	<chem>CC1(C(C(C2=C1C(=C(C(=C2Br)Br)Br)Br)(C)C3=C(C=C(C=C3Br)Br)Br)Br)C</chem>
2 1084889-51-9	4,5,6,7-Tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene	Octalnd	<chem>CC1(CC(C2=C1C(=C(C(=C2Br)Br)Br)Br)(C)C3=CC(=C(C(=C3Br)Br)Br)Br)C</chem>
3 155613-93-7	1H-Indene, 2,3-dihydro-1,1,3-trimethyl-3-phenyl-, octabromo deriv.	OBTMI	<chem>CC1(C2=C(C(=C(C(=C2Br)Br)Br)Br)C(C1(Br)Br)(C)C3=C(C(=CC=C3)Br)Br)C</chem>
4 893843-07-7	4,5,6,7-Tetrabromo-1,1,3-trimethyl-3-(2,3,4,6-tetrabromophenyl)-2,3-dihydro-1H-indene	NA	<chem>CC1(CC(C2=C1C(=C(C(=C2Br)Br)Br)Br)(C)C3=C(C(=C(C=C3Br)Br)Br)Br)C</chem>

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

5.1.2 Polyhalogenated Aliphatic Carboxylate Subclass Chemistry

The PHACbx subclass consists of chemicals whose main functional group is an ester group. The chemicals below are halogenated aliphatic esters with the general formula of RCOOR. They can also be described as carboxylate esters that have a carbonyl carbon (R-C = O) bonded to an OR' group. R and R' represent aliphatic chains. Table 5-2 lists the three individual chemicals in the PHACbx subclass.

Table 5-2. List of Chemicals in Polyhalogenated Aliphatic Carboxylate Subclass

CAS RN	Chemical Name	Abbreviation /Synonyms	SMILES
1 19660-16-3	2,3-Dibromopropyl acrylate	BRN 1762849	<chem>C=CC(=O)OCC(CBr)Br</chem>
2 3066-70-4	2,3-Dibromopropylmethacrylate	NA	<chem>CC(=C)C(=O)OCC(CBr)Br</chem>
3 5445-17-0	Propanoic acid, 2-bromo-, methyl ester	NA	<chem>CC(C(=O)OC)Br</chem>

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

5.1.3 Polyhalogenated Triazine Subclass Chemistry

The PHT subclass consists of polyhalogenated chemicals containing a 1,3,5-triazine substructure. Triazine is a nitrogen containing aromatic heterocycle. The various chemicals in this class were made by substitutions on the N- and/or C- positions of the triazine molecule by halogens or other halogenated functional groups. Table 5-3 lists the six individual chemicals in the subclass.

Table 5-3. List of Chemicals in Polyhalogenated Triazine Subclass

CAS RN	Chemical Name	Abbreviation /Synonyms	SMILES
1 114955-21-4	diethyl (4,6-dichloro-1,3,5-triazin-2-yl)phosphonate	NA	<chem>CCOP(=O)(C1=NC(=NC(=N1)Cl)Cl)OCC</chem>
2 25713-60-4	2,4,6-Tris-(2,4,6-tribromophenoxy)-1,3,5-triazine	NA	<chem>C1=C(C=C(C(=C1Br)OC2=NC(=NC(=N2)OC3=C(C=C(C(=C3Br)Br)Br)OC4=C(C=C(C(=C4Br)Br)Br)Br)Br)Br</chem>
3 52434-59-0	1,3,5-Triazine, 2,4,6-tris(2,3-dibromopropoxy)-	NA	<chem>C(C(CBr)Br)OC1=NC(=NC(=N1)OCC(CBr)Br)OCC(CBr)Br</chem>
4 52434-90-9	1,3,5-Tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione	NA	<chem>C(C(CBr)Br)N1C(=O)N(C(=O)N(C1=O)CC(CBr)Br)CC(CBr)Br</chem>
5 57829-89-7	1-(2,3-dibromopropyl)-3,5-di(prop-2-en-1-yl)-1,3,5-triazinane-2,4,6-trione	NA	<chem>C=CCN1C(=O)N(C(=O)N(C1=O)CC(CBr)Br)CC=C</chem>
6 75795-16-3	1,3-bis(2,3-dibromopropyl)-5-(prop-2-en-1-yl)-1,3,5-triazinane-2,4,6-trione	NA	<chem>C=CCN1C(=O)N(C(=O)N(C1=O)CC(CBr)Br)CC(CBr)Br</chem>

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

5.1.4 Physicochemical Property Summaries

Estimated physicochemical properties were available for chemicals in all three of these subclasses, but measured physicochemical property data was not readily identified from data sources searched.

5.2 Market and Use Summary for Polyhalogenated Benzene Alicycles, Polyhalogenated Aliphatic Carboxylates, and Polyhalogenated Triazines

Four chemicals are in the polyhalogenated benzene alicycle subclass. Two of the chemicals are referenced in the literature and have patent data. One of these chemicals is listed on the Toxic Substances Control Act (TSCA) active inventory. Although there is evidence that these chemicals are used as flame retardants, readily available data describing uses and applications in products were not identified. Exposure assessment could proceed, assuming presence in likely products and modeling all outcomes, but would be highly uncertain.

Three chemicals are in the polyhalogenated aliphatic carboxylate subclass. All three were listed on the TSCA inventory or on other international inventories, and all three have patent data. There is readily available evidence that these chemicals are used as flame retardants with limited data available on specific uses and applications in products. Exposure assessment could proceed for this class in accordance with available market-use information.

Six chemicals are in the polyhalogenated triazine subclass. Two of the six are on the TSCA inventory or on other international inventories, and all six have patent or literature data. There is readily available evidence that these chemicals are used as flame retardants with limited data available on specific uses and applications in products. Exposure assessment could proceed for this class in accordance with available market-use information.

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.⁸ 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.

⁸ See [evidence map files](#).

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

- Limited toxicity data were available, compared with other subclasses.
- PHBA members 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene and 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,6-tetrabromophenyl)-2,3-dihydro-1H-indene had the most data sources in this subclass with 30 and 22 sources, respectively, across all toxicity data categories at 3B review.
- QSAR-Endocrine Disruption was the subcategory with the highest counts of data sources for each of the four PHBA members (QSAR = quantitative structure activity relationships).

5.3.1 Summary of Level 2

The “Integrated” tab contains summed Level 2 toxicity data counts across PDF and database data.⁹ The literature survey identified two to seven integrated data sources (sum of databases and PDFs) for each of the three PHBA members. Table 5-4 summarizes how many PHBA members had different degrees of data source abundance.

Table 5-4. Distribution of Toxicity Data Source Abundance Levels at Level 2

Distribution of Number of Data Sources Available for Each Member	Number of Members with Level 2 Exposure Data Sources	
	PHBA Members (n = 4)	
21+	0	
6–20	1	
1–5	3	
0	0	

5.3.2 Summary of Levels 3 and 3B

The “TOX_Integrated” tabs from each file contain Level 3 and Level 3B toxicity data counts across all toxicity databases and PDFs.¹⁰ Integrated Level 3B counts report the sum of data sources from databases and a sample of up to 25 selected PDFs (i.e., not all PDFs identified at Level 3 were reviewed at Level 3B). The integrated counts indicate the number of data sources per chemical from databases and PDFs identified and classified into seven toxicity data type categories. At Level 3B, reviewers tagged the data sources from each category with subcategories to provide additional details of specific data types. Table 5-5 summarizes how many PHBA members had different degrees of Level 3 toxicity data source abundance.

⁹ See [PHBA Level 2 Evidence Maps, Tab: Integrated](#).

¹⁰ See [PHBA Level 3 Evidence Maps, Tab: TOX Integrated](#) and [PHBA Level 3B Evidence Maps, Tab: TOX Integrated](#).

No toxicity data sources were found for the PHBA class members for the categories *Animal Toxicity or Accepted Alternative*, *Human Toxicity*, *Experimental Mechanistic*, *Qualitative Hazard Characterization*, and *Quantitative Hazard Characterization*.

Table 5-5 Distribution of Toxicity Data Source Abundance Levels at Level 3

Distribution of Number of Data Sources Available for Each Member	Number of Members with Level 3 Toxicity Data Sources PHBA Members (n = 4)						
	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	1	0	0
6–20	0	0	0	0	2	0	0
1–5	0	0	4	0	0	0	0
0	4	4	0	4	1	4	4

Human, Animal, or Modeled Toxicokinetics (ADME [absorption, distribution, metabolism, and excretion]) data sources were available for all four PHBA members at Level 3 review. Two PHBA members 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 PBPK [physiologically based pharmacokinetic] Model; and Chemical- or Class-Specific QSAR for an ADME Parameter. CPSC staff observed the following:

- Of the subcategories, data sources were only found for Human Absorption, Distribution, Excretion and Chemical or Class-Specific QSAR for an ADME Parameter.
- PHBA member 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene had two data sources in the subcategory Human Absorption, Distribution, Excretion and one data source in Chemical- or Class-Specific QSAR for an ADME Parameter.
- PHBA member 1H-indene, 2,3-dihydro-1,1,3-trimethyl-3-phenyl-, octabromo derivative had one data source in the subcategory Human Absorption, Distribution, Excretion.

QSAR, Read-Across, Analog data sources were available for three of the four PHBA members at Level 3 review. All four PHBA members had data in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail for nine subcategories: Acute Toxicity, Systemic or Repeated Dose Toxicity, Neurotoxicity, Carcinogenicity, Mutagenicity/Genotoxicity,

Reproductive Toxicity/Developmental Toxicity, Irritation, Sensitization, and Endocrine Disruption. CPSC staff observed the following:

- No data sources were found for subcategories Systemic or Repeated Dose Toxicity, Neurotoxicity, or Sensitization.
- All four PHBA members had data sources under the subcategories Carcinogenicity (n = 1 or 2 per chemical), Mutagenicity/ Genotoxicity (n = 4 to 8 per chemical), Irritation (n = 1 per chemical, and Endocrine Disruption (n = 6 to 13 per chemical).
- Three of the four PHBA members had one or two data sources per chemical under Acute Toxicity and Reproductive Toxicity/Developmental Toxicity; 1H-indene, 2,3-dihydro-1,1,3-trimethyl-3-phenyl-, octabromo derivative was the PHBA member without data sources in these two subcategories.

5.4 Polyhalogenated Benzene Alicycles 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.¹¹ Level 3B tagging was performed on a subset of up to 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. PHBA 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:

- All four PHBA members had some exposure data.
- 1H-Indene, 2,3-dihydro-1,1,3-trimethyl-3-phenyl-, octabromo derivative had the highest number of exposure data sources among PHBA members.
- PHBA member 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene had data sources across the most exposure categories.

5.4.1 Summary of Level 2

The “Integrated” tab contains summed Level 2 exposure data counts across PDF and database data.¹² The literature survey identified two to 12 integrated data sources (sum of databases and PDFs) for each of the four PHBA members. Table 5-6 summarizes how many PHBA members had different degrees of data source abundance.

¹¹ See [evidence map files](#).

¹² See [PHBA Level 2 Evidence Maps, Tab: Integrated](#).

Table 5-6. Distribution of Exposure Data Source Abundance Levels at Level 2

Distribution of Number of Data Sources Available for Each Member	Number of Members with Level 2 Exposure Data Sources	
	PHBA Members (n = 4)	
21+	0	
6–20	1	
1–5	3	
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.¹³ 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 up to 25 selected PDFs. At Level 3B, reviewers tagged the data sources to subcategories to provide additional details of specific data types. Table 5-7 summarizes how many PHBA members had different degrees of Level 3 exposure data source abundance.

Table 5-7 Distribution of Exposure Data Source Abundance Levels at Level 3

Distribution of Number of Data Sources Available for Each Member	Number of Members with Level 3 Toxicity Data Sources					
	PHBA Members (n = 4)					
	Environmental Monitoring	Biomonitoring/ Personal Monitoring	Source Characterization	Epidemiology – Population Group	Modeled Concentrations	Modeled Human Dose
21+	0	0	0	0	0	0
6–20	1	0	1	0	0	0
1–5	1	4	3	1	0	0
0	2	0	0	3	4	4

No data sources were found for the PHBA class members at levels 3 or 3B for the exposure categories *Modeled Concentrations* and *Modeled Human Dose*.

¹³ See [PHBA Level 3 Evidence Maps](#) and [PHBA Level 3B Evidence Maps](#).

Environmental Monitoring data sources were available for two PHBA members at both Level 3 and 3B reviews. This category was separated into six subcategories for Level 3B review: Indoor/Personal Air, Indoor Dust, Outdoor Air, Food/Dietary, Soil, and Drinking Water. CPSC staff observed the following:

- No data sources were available for subcategories Indoor/Personal Air, Outdoor Air, Soil, or Drinking Water.
- Two PHBA members, 1H-indene, 2,3-dihydro-1,1,3-trimethyl-3-phenyl-, octabromo derivative and 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene had data sources in the Indoor Dust subcategory (n = 4 and 2, respectively).
- PHBA member 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene had one data source under the Food/Dietary subcategory.

Biomonitoring/Personal Monitoring data sources were available for all four PHBA members at Level 3 review. Two PHBA 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). CPSC staff observed the following:

- Subcategories Urine and Skin/Dermal had no data sources for any PHBA members.
- The remaining subcategories Blood/Serum, Breast Milk/Lipids, Skin/Dermal, Human (Other) had data sources for one PHBA member.
- PHBA member 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene had data sources under the Blood/Serum (n = 2) and Breast Milk/Lipids (n = 1) subcategories.
- PHBA member 1H-indene, 2,3-dihydro-1,1,3-trimethyl-3-phenyl-, octabromo derivative had one data source under the Human (Other) category.

Source Characterization data sources were available for all four PHBA members at each Level 3 and 3B reviews. 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. CPSC staff observed the following:

- Subcategories Product Testing: Content Only and Product Testing: Emission/Migration Data had no data sources for any PHBA members.
- All four PHBA members had one to three data sources in the subcategories Nonexperimental Product or Chemical Specific Modeling Inputs and Other Qualitative or Quantitative Description of Product Use or Class/Chemical.

*Environmental Epidemiology*¹⁴ data sources were available for one PHBA member at each Level 3 and 3B reviews. This category was separated into three subcategories for Level 3B

¹⁴ The category *Environmental Epidemiology* here was identified as “*Epidemiology – POP Group*” in the “EXP_Integrated_C” tab of [PHBA Level 3B Evidence Maps](#). The change was made in this document for clarity.

review: Children; Adult, Non-Occupational; and Other, Specify (with Suggestions). CPSC staff observed the following:

- Subcategory Other, Specify (with Suggestions) had no data sources for any PHBA members.
- Subcategories Children and Adult, Non-Occupational each had one data source for PHBA member 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene.

5.5 Polyhalogenated Benzene Alicycles Literature Survey Results: Summary of Existing Human Health Risk Assessments

No chemicals in the PHBA subclass had readily identifiable human health risk assessments.

5.6 Polyhalogenated Aliphatic Carboxylates 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.¹⁵ The database counts indicate either the number of sources within the database (if available) or the number of entries in the database (if no information on source is available) after attempts were made to remove duplicates. The unit for PDF counts is the individual PDF file. Level 3B tagging was performed on a subset of toxicity assessments, toxicity literature reviews, and risk assessments selected from Level 3 to identify even more specific information for the chemicals in these references. Note that most of the Level 3B data are from database data, and only a subset of the PDF data sources is tagged at Level 3B.

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

- All Exposure data categories except *QSAR*, *Read-across*, *Analog* were sparse in data sources for the three PHACbx members and 33 analogs.
- The *QSAR*, *Read-across*, *Analog* category (*QSAR* = quantitative structure activity relationships) had broad representation with 100% of PHACbx members and 100% of analogs having at least one data source at Level 3 review and similar representation at Level 3B.

5.6.1 Summary of Level 2

The “Integrated” tab contains summed Level 2 toxicity data counts across PDF and database data.¹⁶

The literature survey identified integrated data sources (sum of databases and PDFs) for all three PHACbx members and for all 33 analogs. The PHACbx member with the most data

¹⁵ See [evidence map files](#).

¹⁶ See [PHACbx Level 2 Evidence Maps 12.6.22, Tab: Integrated](#).

sources was 2,3-Dibromopropyl acrylate. Table 5-8 summarizes how many PHACbx members and analogs had different degrees of data source abundance.

Table 5-8. 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	
	PHACbx Chemicals (n = 3)	Analog Chemicals (n = 33)
21+	0	0
6–20	1	0
1–5	2	33
0	0	0

5.6.2 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.¹⁷ The Level 3B tabs were divided into A, B, and C to keep the spreadsheets manageable. Integrated Level 3B counts report the sum of data sources from databases and a sample of 25 selected PDFs (i.e., not all PDFs identified at Level 3 were reviewed at Level 3B). The integrated counts indicate the number of data sources per chemical from databases and PDFs identified and classified into seven toxicity data type categories. At Level 3B, reviewers tagged the data sources from each category with subcategories to provide additional details of specific data types. Table 5-9 and Table 5-10 summarize how many PHACbx members and analogs had different degrees of Level 3 toxicity data source abundance.

¹⁷ See [PHACbx Level 3 Evidence Maps](#), Tab: TOX Integrated and [PHACbx Level 3B Evidence Maps](#), Tab: TOX Integrated.

Table 5-9. 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						
	PHACbx Chemicals (n = 3)						
	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	1	3	0	0
6–20	2	0	0	0	0	1	1
1–5	1	0	3	1	0	2	0
0	0	3	0	1	0	0	2

Table 5-10. 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						
	PHACbx Analogs (n = 33)						
	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	1	11	0	0
6–20	0	0	0	1	0	0	0
1–5	1	0	11	3	22	0	1
0	32	33	22	28	0	33	32

No data sources were available for PHACbx members or analogs at Level 3 or 3B for the *Human Toxicity* category.

Animal Toxicity or Accepted Alternative data sources were available for all three PHACbx members and one analog at Level 3 review and in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail for nine subcategories: Acute Toxicity, Systemic or Repeated Dose Toxicity, Neurotoxicity, Carcinogenicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental Toxicity, Irritation, Sensitization, and Endocrine Disruption. CPSC staff observed the following:

- PHACbx member 2,3-Dibromopropyl acrylate had data sources in the subcategories Systemic or Repeated Dose Toxicity, Mutagenicity/Genotoxicity, and Reproductive Toxicity/Developmental Toxicity.
- PHACbx member 2,3-Dibromopropylmethacrylate had data sources only in the Mutagenicity/Genotoxicity subcategory.
- PHACbx member Propanoic acid, 2-bromo-, methyl ester had data sources only in the Irritation subcategory.
- Analog Methyl 2,3-dibromopropionate had data sources in the Acute Toxicity Mutagenicity/Genotoxicity, and Irritation subcategories.

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

- PHACbx members propanoic acid, 2-bromo-, methyl ester; 2,3-dibromopropyl acrylate; and 2,3-dibromopropylmethacrylate and 11 analogs had data sources in the Chemical- or Class-Specific QSAR for an ADME Parameter subcategory.
- The remaining subcategories had no data sources for any of the PHACbx members or analogs.

Experimental Mechanistic data sources were available for two PHACbx members and five analogs at Level 3 review. One PHACbx member and one analogs had data in the databases and PDFs at Level 3B review.¹⁸ This category had two subcategories at Level 3B review

¹⁸ See “TOX_DB” and “TOX_PDF” tabs of [PHACbx Level 3B Evidence Map](#). 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.

separating those data sources that make a connection to mode of action (MOA) and a potential health effect from those that do not.¹⁹ CPSC staff observed the following:

- PHACbx member 2,3-dibromopropyl acrylate had 420 data sources in the subcategory Study Makes Connection to MOA and Potential Health Effect.
- Analog methyl 2,3-dibromopropionate had 163 data sources in the subcategory Study Makes Connection to MOA and Potential Health Effect.
- The subcategory Study Does Not Makes Connection to MOA and Potential Health Effect had no data sources for PHACbx members or analogs.

QSAR, Read-Across, Analog data sources were available for all three PHACbx members and all 33 analogs at Level 3 review and in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail across the same nine subcategories used for *Animal Toxicity or Accepted Alternative* above. CPSC staff observed the following:

- No data sources for PHACbx members or analogs were identified for Neurotoxicity. The vast majority of 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.
- PHACbx member propanoic acid, 2-bromo-, methyl ester and six analogs had data sources in all subcategories except Neurotoxicity.
- PHACbx members 2,3-dibromopropyl acrylate; and 2,3-dibromopropylmethacrylate and two analogs had data sources in all subcategories except Systemic or Repeated Dose Toxicity and Neurotoxicity.
- Subcategories Acute Toxicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental Toxicity, and Endocrine Disruption had data sources for all three PHACbx members and all 33 analogs.

¹⁹ Many database sources could not be tagged for Level 3B because it was not clear whether a connection was made to MOA.

Qualitative Hazard Characterization data sources were available for all three PHACbx members and no analogs at Level 3 review and 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. (For example, 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:

- PHACbx member 2,3-Dibromopropyl acrylate had data sources for the subcategories Acute Toxicity, Mutagenicity/Genotoxicity, and Irritation.
- PHACbx member 2,3-Dibromopropylmethacrylate had data sources only in the subcategory Mutagenicity/Genotoxicity.
- PHACbx member Propanoic acid, 2-bromo-, methyl ester had data sources only in the Irritation subcategory.

Quantitative Hazard Characterization data sources were available for one PHACbx member and one analog at Level 3 review and 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:

- PHACbx member 2,3-Dibromopropyl acrylate had data sources available in the Systemic Repeated Dose Toxicity, and Reproductive Toxicity/Developmental Toxicity subcategories.
- Analog Methyl 2,3-dibromopropionate had one data source in the Acute Toxicity subcategory.

5.7 Polyhalogenated Aliphatic Carboxylates 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.²⁰ 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. PHACbx analogs were not included in the exposure evidence map analyses because exposure to the analogs is outside the scope of the current project.

²⁰ See [evidence map files](#).

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

- Each of the three PHACbx members had one data source in the Source Characterization category.
- This subclass is data poor for exposure data.

5.7.1 Summary of Level 2

The MMDB database and PDF searches identified exposure data sources for all eight PHACbx members.²¹ Each of the three PHACbx members had one data source. Table 5-11 summarizes how many PHACbx members had different degrees of data source abundance. The PDFs provided the only total data sources available for PHACbx members, and no sources were found in the database.

Table 5-11. 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	
	PHACbx Chemicals (n = 3)	
21+	0	
6–20	0	
1–5	3	
0	0	

5.7.2 Summary of Levels 3 and 3B

The “EXP_Integrated” tabs from each file contains Level 3 and 3B exposure data counts.²² 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 5-12 summarizes how many PHACbx members had different degrees of Level 3 exposure data source abundance.

²¹ See [PHACbx Level 2 Evidence Map file](#).

²² See [PHACbx Level 3 Evidence Map](#) and [PHACbx Level 3B Evidence Map](#).

Table 5-12. 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					
	PHACbx Chemicals (n = 3)					
	Environmental Monitoring	Biomonitoring/ Personal Monitoring	Source Characterization	Epidemiology – Population Group	Modeled Concentrations	Modeled Human Dose
21+	0	0	0	0	0	0
6–20	0	0	0	0	0	0
1–5	0	0	3	0	0	0
0	3	3	0	3	3	3

No data sources were available for PHT members at Level 3 or 3B for the exposure categories *Environmental Monitoring*; *Biomonitoring/Personal Monitoring*; *Environmental Epidemiology*;²³ *Modeled Concentrations*; or *Modeled Human Dose*.

Source Characterization data sources were available for all three PHACbx members at Level 3 review and 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. The three PHACbx members 2,3-Dibromopropylmethacrylate; Propanoic acid, 2-bromo-, methyl ester; and 2,3-Dibromopropyl acrylate each had one data source in the Other Qualitative or Quantitative Description of Product Use or Class/Chemical subcategory.

5.8 Polyhalogenated Aliphatic Carboxylates Literature Survey Results: Summary of Existing Human Health Risk Assessments

No chemicals in the PHACbx subclass had readily identifiable human health risk assessments.

5.9 Polyhalogenated Triazines 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.²⁴ The database counts indicate either

²³ The category *Environmental Epidemiology* here was identified as “*Epidemiology – POP Group*” in the “EXP_Integrated_C” tab of [PHACbx Level 3B Evidence Map](#). The change was made in this document for clarity.

²⁴ See [evidence map files](#).

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

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

- PHT members 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione and 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had the highest number of data sources in each category for which data were available and the most representation across exposure categories for database and PDF reviews.
- The QSAR, Read-across, Analog category (QSAR = quantitative structure activity relationships) had broad representation with 100% of PHT members and 100% of analogs having at least one data source at Level 3 review and similar representation at Level 3B.
- The analog 2,4,6-tris(2,4-dibromophenoxy)-1,3,5-triazine did not have more data sources than any of the PHT members.

5.9.1 Summary of Level 2

The “Integrated” tab contains summed Level 2 toxicity data counts across PDF and database data.²⁵

The literature survey identified integrated data sources (sum of databases and PDFs) for all eight PHT members and for 30 of 32 analogs. The PHT members with the most data sources were 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione and 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine. Table 5-13 summarizes how many PHT members and analogs had different degrees of data source abundance.

Table 5-13. 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	
	PHT Chemicals (n = 6)	Analog Chemicals (n = 1)
21+	0	0
6–20	2	0
1–5	4	1
0	0	0

²⁵ See [PHT Level 2 Evidence Maps, Tab: Integrated](#).

5.9.2 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.²⁶ The Level 3B tabs were divided into A, B, and C to keep the spreadsheets manageable. Integrated Level 3B counts report the sum of data sources from databases and a sample of 25 selected PDFs (i.e., not all PDFs identified at Level 3 were reviewed at Level 3B). The integrated counts indicate the number of data sources per chemical from databases and PDFs identified and classified into seven toxicity data type categories. At Level 3B, reviewers tagged the data sources from each category with subcategories to provide additional details of specific data types. Table 5-14 and Table 5-15 summarize how many PHT members and analogs had different degrees of Level 3 toxicity data source abundance.

Table 5-14. 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						
	PHT Chemicals (n = 6)						
	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+	1	0	0	2	4	0	0
6–20	1	0	0	0	2	0	1
1–5	0	0	2	0	0	2	1
0	4	6	4	4	0	4	4

²⁶ See [PHT Level 3 Evidence Maps, Tab: TOX Integrated](#) and [PHT Level 3B Evidence Maps, Tab: TOX Integrated](#).

Table 5-15. 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						
	PHT Analogs (n = 1)						
	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	0	0	0
6–20	0	0	0	0	1	0	0
1–5	0	0	0	0	0	0	0
0	1	1	1	1	0	1	1

No data sources were available for PHT members or analogs at Level 3 or 3B for the *Human Toxicity* category.

Animal Toxicity or Accepted Alternative data sources were available for two PHT members and no analogs at Level 3 review and in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail for nine subcategories: Acute Toxicity, Systemic or Repeated Dose Toxicity, Neurotoxicity, Carcinogenicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental Toxicity, Irritation, Sensitization, and Endocrine Disruption. CPSC staff observed the following:

- PHT member 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione had data sources for all subcategories except Sensitization.
- PHT member 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had data sources for all subcategories except Neurotoxicity, Carcinogenicity, and Endocrine Disruption.
- The analog 2,4,6-tris(2,4-dibromophenoxy)-1,3,5-triazine had no data sources in this category.

Human, Animal, or Modeled Toxicokinetics (ADME [absorption, distribution, metabolism, and excretion]) data sources were available for two PHT members and no analogs at Level 3 review and in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail on seven subcategories: Human Absorption, Distribution, Excretion; Animal Absorption, Distribution, Excretion; Human Metabolism; Animal Metabolism; In Vitro; Chemical- or Class-

Specific PBPK [physiologically based Pharmacokinetic] Model; and Chemical- or Class-Specific QSAR for an ADME Parameter. CPSC staff observed the following:

- PHT member 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione had data sources in the subcategories Human Absorption, Distribution, Excretion; Animal Absorption, Distribution, Excretion; and Chemical- or Class-Specific QSAR for an ADME Parameter.
- PHT member 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had data sources in the Chemical- or Class-Specific QSAR for an ADME Parameter subcategory.
- The analog 2,4,6-tris(2,4-dibromophenoxy)-1,3,5-triazine had no data sources in this category.

Experimental Mechanistic data sources were available for two PHT members and no analogs at Level 3 review and in the databases and PDFs at Level 3B review.²⁷ This category had two subcategories at Level 3B review separating those data sources that make a connection to MOA and a potential health effect from those that do not.²⁸ CPSC staff observed the following:

- PHT member 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione had data sources in both subcategories.
- PHT member 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had data sources in the subcategory Study Makes Connection to MOA and Potential Health Effect.
- The analog 2,4,6-tris(2,4-dibromophenoxy)-1,3,5-triazine had no data sources in this category.

QSAR, Read-Across, Analog data sources were available for all six PHT members and the one analog at Level 3 review and in the databases and PDFs at Level 3B review. Level 3B reviews provided additional detail across the same nine subcategories used for *Animal Toxicity or Accepted Alternative* above. CPSC staff observed the following:

- PHT members 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had data sources in all subcategories except Systemic Repeated Dose Toxicity.
- PHT member 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione had data sources in all subcategories except Systemic Repeated Dose Toxicity and Neurotoxicity.
- The subcategories Acute Toxicity, Mutagenicity/Genotoxicity, Reproductive Toxicity/Developmental [Toxicity], and Endocrine Disruption had data sources for all six PHT members and the analog.

Qualitative Hazard Characterization data sources were available for two PHT members and no analogs at Level 3 review and in the databases and PDFs at Level 3B review. In contrast with

²⁷ See “TOX_DB” and “TOX_PDF” tabs of [PHT Level 3B Evidence Map](#). 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.

²⁸ Many database sources could not be tagged for Level 3B because it was not clear whether a connection was made to MOA.

all other data types, a tag for Qualitative Hazard Characterization indicates that a review/assessment was attempted, not necessarily that data were found. (For example, 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:

- PHT member 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had one to three data sources for each of the nine subcategories.
- PHT member 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione had one to two data sources in all subcategories except Systemic Repeated Dose Toxicity and Sensitization.
- The analog 2,4,6-tris(2,4-dibromophenoxy)-1,3,5-triazine had no data sources in this category.

Quantitative Hazard Characterization data sources were available for two PHT members and no analogs at Level 3 review and 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, Sensitization, and Endocrine Disruption. CPSC staff observed the following:

- PHT member 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione had data sources available in the most subcategories. These were Acute Toxicity, Systemic Repeated Dose Toxicity, Reproductive Toxicity/Developmental [Toxicity], and endocrine disruption.
- PHT member 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had one to seven data sources in the subcategories Acute Toxicity, Systemic or Repeated Dose Toxicity, and Reproductive Toxicity/Developmental.
- The analog 2,4,6-tris(2,4-dibromophenoxy)-1,3,5-triazine had no data sources in this category.

5.10 Polyhalogenated Triazines 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.²⁹ 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. PHT analogs were not included in the exposure evidence map analyses because exposure to the analogs is outside the scope of the current project.

²⁹ See [evidence maps](#).

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

- PHT member 1,3,5-Tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione had data sources in each category for which data were available.
- PHT members 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione and 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine had the most representation across two exposure categories for which data were available for database and PDF reviews.

5.10.1 Summary of Level 2

The MMDB database and PDF searches identified exposure data sources for all eight PHT members.³⁰ The PHT members with the most data sources were 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione and 2,4,6-tris-(2,4,6-tribromophenoxy)-1,3,5-triazine. Table 5-16 summarizes how many PHT members had different degrees of data source abundance. The PDFs provided more total data sources and covered more PHT members than the database.

Table 5-16. 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	
	PHT Chemicals (n = 6)	
21+	0	
6–20	1	
1–5	3	
0	2	

5.10.2 Summary of Levels 3 and 3B

The “EXP_Integrated” tabs from each file contains Level 3 and 3B exposure data counts.³¹ 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 5-17 summarizes how many PHT members had different degrees of Level 3 exposure data source abundance.

³⁰ See [PHT Level 2 Evidence Maps](#).

³¹ See [PHT Level 3 Evidence Map](#) and [PHT Level 3B Evidence Map](#).

Table 5-17. 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					
	PHT Chemicals (n = 6)					
	Environmental Monitoring	Biomonitoring/Personal Monitoring	Source Characterization	Epidemiology – Population Group	Modeled Concentrations	Modeled Human Dose
21+	0	0	0	0	0	0
6–20	1	0	1	0	0	0
1–5	1	0	3	0	0	0
0	2	6	2	6	6	6

No data sources were available for PHT members at Level 3 or 3B for the exposure categories *Biomonitoring/Personal Monitoring*; *Environmental Epidemiology*;³² *Modeled Concentrations*; or *Modeled Human Dose*.

Environmental Monitoring data sources were available for two PHT members at Level 3 review and 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.

- PHT member 2,4,6-tribromophenol had sources in all of the subcategories.
- PHT member 1,3,5-triazine, 2,4,6-tris(2,3-dibromopropoxy)- had data sources in the Soil and Drinking Water subcategories.
- PHT member diethyl (4,6-dichloro-1,3,5-triazin-2-yl)phosphonate had a data source for Outdoor Air only.

Source Characterization data sources were available for six PHT members at Level 3 review and 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. PHT members diethyl (4,6-dichloro-1,3,5-triazin-2-yl)phosphonate; 1,3,5-triazine, 2,4,6-tris(2,3-dibromopropoxy)-; 1,3,5-tris(2,3-dibromopropyl)-1,3,5-triazine-2,4,6(1H,3H,5H)-trione; and 1-

³² The category *Environmental Epidemiology* here was identified as “*Epidemiology – POP Group*” in the “EXP_Integrated_C” tab of [PHT Level 3B Evidence Map](#). The change was made in this document for clarity.

(2,3-dibromopropyl)-3,5-di(prop-2-en-1-yl)-1,3,5-triazinane-2,4,6-trione each had data sources in the Other Qualitative or Quantitative Description of Product Use or Class/Chemical subcategory.

5.11 Polyhalogenated Triazines Literature Survey Results: Summary of Existing Human Health Risk Assessments

No chemicals in the PHT subclass had readily identifiable human health risk assessments.

5.12 Literature Survey Results: Key References

No key authoritative sources were readily identified for the PHBA, PHACbx, or PHT subclasses.

6. Scoping Determination and Next Steps

6.1. Scoping Determination

The primary objective of completing a literature survey 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 as long as 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 final section of the scope document includes initial observations informed by review of select data sources.

6.1.1. Polyhalogenated Benzene Alicycles

Toxicity data on the PHBA subclass are extremely limited. No empirical toxicity data were located for any class member, and no analogs were identified for this class. The only available hazard data were biomonitoring measurements (indicating that the chemical is absorbed) and in silico toxicity predictions for 4,5,6,7-tetrabromo-1,1,3-trimethyl-3-(2,3,4,5-tetrabromophenyl)-2,3-dihydro-1H-indene (OBTMPI) (Das et al., 2021). This study reported that OBTMPI, and its possible metabolites in humans, were unlikely to be carcinogenic or mutagenic but may have some endocrine disrupting properties based on estrogen antagonist, androgen antagonist, and estrogen binding capability. Overall, the data at the time of writing appear to be insufficient to proceed with a class-based risk assessment for PHBAs.

6.1.2. Polyhalogenated Aliphatic Carboxylates

Toxicity data on the PHACbx subclass are extremely limited. No PDFs with toxicity data were located for any class member, although some database data were located. Most of the database data were mechanistic or QSAR-based, but some empirical database data were identified for all three class members and five analogs. Most of the empirical database data

were from the OECD Toolbox, ToxVal, ICE, or PubChem Bioassay. The vast majority of the data were experimental mechanistic data, although there were also some genotoxicity data and data from unpublished studies. Overall, the data at the time of writing appear to be insufficient to proceed with a class-based risk assessment for the polyhalogenated aliphatic carboxylates.

6.1.3. Polyhalogenated Triazines

Tris(2,3-dibromopropyl) isocyanurate (TDBP-TAZTO) appears to be essentially nonlethal when administered orally to rats and mice (LD50 > 15,000 mg/kg; Dong et al., 2021). 2,4,6-Tris(2,4,6-tribromophenoxy)-1,3,5-triazine (TTBP-TAZ) also appears to have low acute toxicity to rats via both oral and dermal routes (LD50 > 2,000 mg/kg; U.S. EPA, 2014), although this empirical result is in conflict with modeled results, for which the average of three different *in silico* models predicted an oral LD50 of ~275 mg/kg (Zheng et al., 2019).

EFSA (2012) identified no hazard characterization information on 1-(2,3-dibromopropyl)-3,5-diallyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (DBP-TAZTO) or 1,3-bis(2,3-dibromopropyl)-5-allyl-1,3,5-triazine-2,4,6(1H,3H,5H)-trione (BDBP-TAZTO).

Studies longer than acute duration were identified only for TDBP-TAZTO and TTBP-TAZ. TTBP-TAZ had no treatment-related effects in a 28-day rat study (U.S. EPA, 2014). TDBP-TAZTO affected the liver in a 28-day mouse study (Li et al., 2015; Dong et al., 2021), the (developing) nervous system in a 30-day study in mice and in a 6-month study in rats (Cao et al., 2018; Bar and Szychowski, 2022), and the endocrine system in a 4-week rat study (Zhou et al., 2019). These targets are further supported by *in vitro* and *in silico* studies (Zhou et al., 2019; EFSA, 2012; Bar and Szychowski, 2022; Zheng et al., 2019; Dong et al., 2021; Cao et al., 2018; Bajard et al., 2021).

TDBP-TAZTO may affect the liver, possibly via effects on the mitochondria. Mice exposed via gavage to TDBP-TAZTO for 28 days had histopathological changes in the liver (necrosis, apoptosis, mitochondrial degeneration, and endoplasmic reticulum dilation), increased serum alanine aminotransferase (ALT), and increased p53 gene expression in the liver (Li et al., 2015; Dong et al., 2021). Zebrafish exposed to TDBP-TAZTO had liver damage (adults) and disruption of mitochondrial cristae in the gas bladder (larvae) (EFSA, 2012). *In vitro*, TDBP-TAZTO was not cytotoxic to HepG2 cells (EFSA, 2012). After 4 weeks of exposure to TDBP-TAZTO, rats had reduced serum levels of ALT and aspartate aminotransferase (AST), and reduced expression of estrogen receptor 1 (ER1) in liver (Zhou et al., 2019). The toxicological significance of the reduced ALT and AST is unclear.

In a 6-month study in adult rats (Cao et al., 2018; Bar and Szychowski, 2022) and in a 30-day study in mice (Bar and Szychowski, 2022), TDBP-TAZTO caused increased inflammation, oxidative stress, and expression of proapoptotic proteins in the brain (in mice, specifically the hippocampus), and associated depressive behavior. The rats also experienced disrupted neurogenesis and cognitive problems (Bar and Szychowski, 2022). Another study found reduced relative brain weights after 4 weeks exposure to TDBP-TAZTO (Zhou et al., 2019). *In vitro*, TDBP-TAZTO was cytotoxic to developing rat cerebellum granule neurons (CGN), but not

mature rat CGN (cells were mature after 7 days in culture) (EFSA, 2012; Bar and Szychowski, 2022).

Several *in silico* predictions suggest TTBP-TAZ may also affect endocrine systems and developmental toxicity (Zheng et al., 2019), although professional judgment-based predictions contradict this suggestion because of low predicted bioavailability (Danish EPA, 2014; U.S. EPA, 2014). U.S. EPA (2014, of which a draft version is cited in Danish EPA, 2014) categorized TTBP-TAZ as “low” concern for reproductive, developmental, neurological, endocrine toxicity, and carcinogenicity according to expert judgment relying on limited estimated bioavailability (based on molecular weight greater than 1,000 daltons unlikely to be bioavailable).

Several studies have investigated the potential androgen- and estrogen-related activity of TDBP-TAZTO. Zebrafish exposed to TDBP-TAZTO had estrogenic effects (72 hours post-fertilization) and anti-estrogenic effects (28 days of exposure) (Dong et al., 2021). In addition to the above reduced expression of ER1 in liver (Zhou et al., 2019), TDBP-TAZTO had anti-estrogenic activity in MCF-7 breast cancer cells and sex hormone synthesis was inhibited in H295R human adenocarcinoma cells (Dong et al., 2021). TDBP-TAZTO also had anti-estrogenic effects *in vitro* via the ER-alpha signaling pathway (Cao et al., 2018). Computational molecular docking and molecular dynamics studies suggest TDBP-TAZTO blocks recruitment of co-activators and transcription by competing for a surface site (rather than the estrogen binding site) of ER-alpha (Cao et al., 2018). TDBP-TAZTO is also predicted to have anti-androgenic activity (Bajard et al., 2021). On the basis of *in silico* predictions, Zheng et al. (2019) categorized TTBP-TAZ as medium-high for androgen binding, medium-low for estrogen binding, low for transthyretin binding, and medium-high for developmental toxicity.

TDBP-TAZTO is listed in the REACH ECHA Annex Inventory III as a suspected mutagen and suspected carcinogen (Zuiderveen et al., 2020), although the basis for this classification is not clear. TTBP-TAZ was negative *in vitro* for bacterial gene mutation and chromosomal aberration (U.S. EPA, 2014). On the basis of *in silico* predictions, Zheng et al. (2019) categorized TTBP-TAZ as low for mutagenicity and medium-low for carcinogenicity.

Overall, it appears there are insufficient data at the time of writing for a class-based assessment of PHTs because of the lack of repeat dose studies of adequate quality and adequate duration. Nearly all empirical data for members of this subclass come from a single chemical, TDBP-TAZTO. Predictions for TTBP-TAZ indicate it may share endocrine system and carcinogenic effects with TDBP-TAZTO, although this is highly uncertain. It may be appropriate to combine at least some members of this class with other subclasses for an analysis, but specific recommendations would require a more detailed investigation. Grouping some or all of the polyhalogenated triazines with members of other classes may allow for a class-based risk assessment.

6.2. Next Steps

CPSC staff determined there is insufficient information to proceed with a class-based risk assessment for these subclasses at this time.

CPSC staff will continue to monitor available information in the literature and from governmental organizations to determine whether new data become available that would make it possible to proceed with a class-based assessment.

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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

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Organohalogen Flame Retardant Scope Document: Polyhalogenated Benzene Alicycle, Polyhalogenated Aliphatic Carboxylate, and Polyhalogenated Triazine Subclasses

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