Staff Briefing Package

Project Plan: Organohalogen Flame Retardant Chemicals Assessment

July 1, 2020

Acknowledgments

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Briefing Memo

UNITED STATES
CONSUMER PRODUCT SAFETY COMMISSION
4330 EAST WEST HIGHWAY
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Memorandum

Date: July 1, 2020

TO: The Commission
Alberta E. Mills, Secretary

THROUGH: John G. Mullan, General Counsel
Mary T. Boyle, Executive Director
DeWane Ray, Deputy Executive Director for Safety Operations

FROM: Duane Boniface, Assistant Executive Director
Office of Hazard Identification and Reduction
Kristina M. Hatlelid, Ph.D., M.P.H., Project Manager
Division of Toxicology and Risk Assessment, Directorate for Health Sciences

SUBJECT : Project Plan: Organohalogen Flame Retardant Chemicals Assessment

1. Executive summary

Recommendations

U.S. Consumer Product Safety Commission (CPSC or Commission) staff's plan for class-based risk assessment of organohalogen flame retardants (OFRs) includes recommendations for proceeding with a number of activities based on recommendations from the National Academy of Sciences, Engineering, and Medicine, in their report to the CPSC, "A Class Approach to Hazard Assessment of Organohalogen Flame Retardants." These activities establish the foundation for initiating and completing risk assessments for OFR subclasses. For fiscal year 2021, CPSC requested a recurring $1.5 million above baseline appropriations in the Performance Budget Request because existing baseline appropriations are insufficient to complete this work. Thus, all plans identified below are contingent upon receiving this additional appropriation and additional appropriations in future years to continue this work.

In fiscal year 2021 (FY 2021), staff will establish procedures for class-based risk assessment of OFRs, will refine the chemicals and analogs for subclasses, identify data sources, and determine available toxicity, chemical use, and exposure information. In addition, staff will begin to develop scope documents and analysis plans for defined chemical subclasses. As these

documents and plans are completed for each subclass, staff will proceed with searching for relevant data and information, and begin to extract, evaluate, and integrate the data to reach decisions about the hazards, exposures, and risks of a class or to identify data gaps and additional data needs. In FY 2021, staff will establish support contracts and interagency agreements for tasks that can be performed by contractors and through interagency collaboration, and will proceed with multiple activities in parallel performed by staff, contractors, and other collaborations.

Background

In 2015, a number of organizations and individuals petitioned the CPSC (Petition HP 15-1) to ban the use of additive OFRs, as a class, in durable infant or toddler products, children's toys, child care 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 (CHAP), and to complete a scoping and feasibility study in cooperation with the National Academy of Sciences, Engineering, and Medicine (NASEM). NASEM published the committee's report, "A Class Approach to Hazard Assessment of Organohalogen Flame Retardants," in May 2019.

Process for Class-Based Risk Assessment

CPSC staff's recommended process for assessing the risks of OFRs is described in this memo and is developed by incorporating established basic principles of risk assessment for chemicals in consumer products. The process includes steps for assessing potential human health effects associated with the chemicals, evaluating exposure to the chemicals from their use in consumer products, and characterizing the risks to consumers. Staff acknowledges that the process for a class-based assessment may differ from a risk assessment for a single chemical. Staff provides an overview of the processes for assessing hazards and exposure, and for characterizing risk. Staff also provides details for specific risk assessment tasks, describes the iterative nature of risk assessments, and describes a tiered-analysis approach that can consider resource and data availability.

Activities to Support Class-Based Risk Assessment

CPSC staff's approaches for inter-related technical support activities required for class-based risk assessment are described in the tabs. Tab A provides details for a class-based hazard assessment, building on the recommendations from the NASEM report. Tab B provides details for completing class-based exposure assessments. Tab C provides details for technical support activities, including examples that provide the foundation for future work. Tab D provides preliminary market-use information for certain OFR chemicals. Tab E provides a glossary of terms.

2. Introduction

This staff report presents background information and an analysis plan for the project on assessing hazards, exposures, and risks of organohalogen flame retardants (OFRs) in consumer products. Staff outlines key steps in the analysis plan and provides options for proceeding with the project. This memo contains a description of activities supporting class-based risk assessments for OFRs. Technical project details are located in the package tabs.

3. Background

In 2015, the CPSC received a request on Consumer Products Containing Additive Organohalogen Flame Retardants. This request was docketed as Petition 15-1, under Commission procedures. The petition and related information are available online in the public docket.[1] The list of petitioners included a number of organizations and individuals, such as consumer organizations, medical associations, worker, and firefighter organizations.

The petition requested that the Commission ban the use of additive, non-polymeric organohalogen flame retardants under the authority of the Federal Hazardous Substances Act in the following categories of consumer products:

- Durable infant or toddler products, children's toys, child care articles, or other children's products (other than car seats, which are under Department of Transportation's jurisdiction);
- Residential upholstered furniture;
- Mattresses and mattress pads; and
- The plastic casings of electronic devices.

The petition scope included OFRs as a class. The petition specified that the scope covered all non-polymeric, additive flame retardants. Additive OFRs are not chemically bound to the four product types containing them. The petitioners maintained that OFRs could be regulated as a class because they are "toxic due to their physical, chemical and biological properties," and there is widespread human exposure. The petitioners explained further that banning OFRs as a class would prevent a cycle of "regrettable substitution."

In September 2017, the Commission voted to grant the petition, to direct staff to convene a CHAP, and to complete a scoping and feasibility study in cooperation with NASEM. The task for this project was to develop a scientifically based scoping plan to identify the potential health hazards associated with additive, nonpolymeric OFRs as a class. The project:

- Surveyed available hazard data for OFRs, and identified data needed for a CHAP to conduct a class-level hazard assessment.
- Identified one or more approaches to scientifically assess the potential for treating OFRs as a single class for purposes of hazard assessment; and
- Provided a plan for how to efficiently and effectively conduct research needed to evaluate OFRs.

[1] https://www.regulations.gov/docket?D=CPSC-2015-0022.

The NASEM committee published the report, "A Class Approach to Hazard Assessment of Organohalogen Flame Retardants," in May 2019.[2]

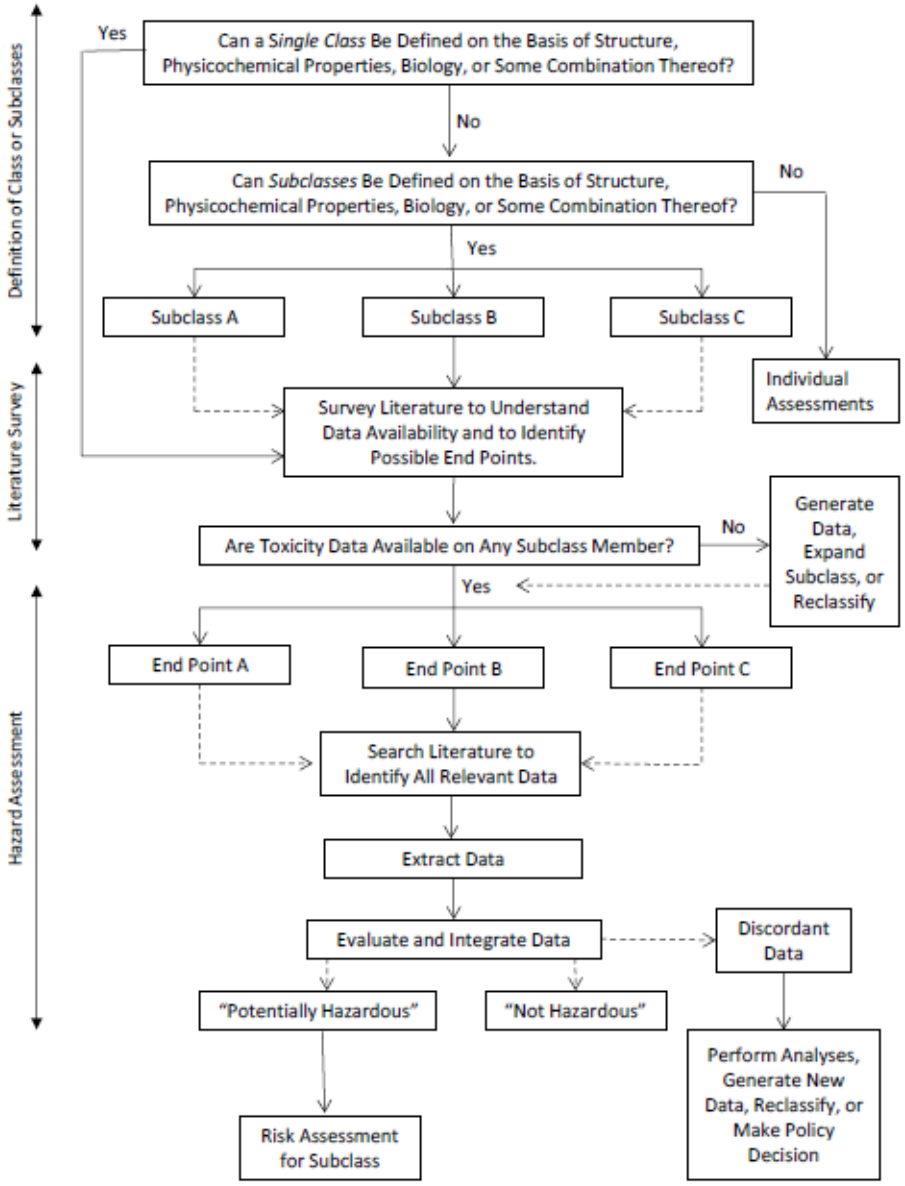
A) NASEM REPORT

The NASEM committee (the Committee) outlined a process for hazard identification for classes of chemicals. Hazard identification is the first step of risk assessment, followed by dose-response assessment, exposure assessment, and risk characterization. Briefly, 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. 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. If relevant data are available on any chemical of interest for a given end point, then 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.

In developing the approach for organohalogen flame retardants, the Committee created an inventory of 161 OFRs, and identified more than 1,000 analogue chemicals (*i.e.*, chemicals with similar functional, structural, and predicted biological activity). 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 biologic activity. The Committee also indicated that the best approach would be to define subclasses as broadly as is feasible for the analysis, because defining subclasses too narrowly could defeat the purpose of a class approach. The Committee's scoping plan is represented in Figure 1.

[2] National Academies of Sciences, Engineering, and Medicine 2019. A Class Approach to Hazard Assessment of Organohalogen Flame Retardants. Washington, DC: The National Academies Press. https://doi.org/10.17226/25412. Available at: http://nap.edu/25412.

Figure 1: Scoping Plan to Conduct a Hazard Assessment for CPSC Using a Class-based Approach



Source: National Academies of Sciences, Engineering, and Medicine 2019. A Class Approach to Hazard Assessment of Organohalogen Flame Retardants. Washington, DC: The National Academies Press. https://doi.org/10.17226/25412. Available at: http://nap.edu/25412.

The Committee then worked through case studies for two subclasses, and identified four possible scenarios that could arise in evaluating subclasses.

Scenario 1: A subclass has many data-rich members and data are concordant, that is, consistent regarding biological activity. The Committee did not identify potential unique challenges for proceeding with an assessment of a subclass under this scenario.

Scenario 2: There are no relevant data on any subclass member that are useful for hazard assessment. The Committee identified possible options for dealing with this case:

Option 2-1: Generate new toxicity data on the subclass.

Option 2-2: Expand the analysis beyond the set of chemicals that were identified as OFRs and use toxicity data on structurally related chemicals (analogues).

Option 2-3: Reclassify the subclass so that data-poor members are distributed in other data-rich subclasses. Many OFRs have multiple functional groups and could be placed in multiple subclasses; reclassification might help to minimize the number of data-poor categories.

Scenario 3: There are sufficient coherent data on one or two chemicals in the group, but few or no data on other class members. The Committee identified a number of options for this scenario:

Option 3-1: Make a science-based policy decision, for example, to classify the subclass as potentially hazardous on the basis of the data-rich chemicals in the subclass.

Option 3-2: Use the data-rich chemicals to serve as an anchor and extrapolate to other chemicals in the subclass.

Option 3-3: Generate toxicity data on data-poor subclass members to the extent that satisfactory confidence is gained.

Scenario 4: There are data for some chemicals in the subclass, and few or no data on others; and the data that are available are so inconsistent with respect to biologic activity that a discordant-data designation is reached. The Committee stated that this case is the most difficult, but, the Committee stated that there may be analyses or testing that can be done to provide enough information for decisions:

Option 4-1: Make a policy decision, for example, to extend the most conservative conclusion[3] regarding hazard to the subclass.

Option 4-2: Reclassify members in such a way that biologic similarity is improved; generate new toxicity data to increase confidence that reclassification has resulted in biologically similar members.

Option 4-3: Perform analyses that would help to explain the discordance and allow the assessment to move forward.

Option 4-4: Generate new toxicity data that could increase clarity and the scientific basis of a decision.

[3] In this context, "conservative" refers to making decisions and conclusions about available data and information that are the most health protective, given a range of possible options.

With respect to generating new toxicity data, the Committee recommended a tiered approach that initially would rely on new approach methodologies (NAMs) that encompass computational modeling, in vitro assays in animal and human cells and tissues, and toxicity testing that uses alternative animal species, such as zebrafish. The Committee concluded that the results of such studies can help to identify potential end points of interest and one or more chemicals in a subclass for targeted animal toxicity studies. Details of toxicity testing are provided in Tab C.

The Committee recognized that CPSC will have to make certain policy decisions regarding the acceptability of relying on NAMs and other non-traditional toxicity data. The Committee concluded: "[i]deally, the class approach provides a mechanism for extrapolating data on data-rich chemicals to data-poor chemicals and eliminates the need to collect data on all chemicals in a specific class."

B) CPSC Activities Related to Flame Retardant Chemicals[4]

CPSC staff has been active in assessing the potential health risks of flame retardant chemicals since the 1970s, including laboratory research and health risk assessments. Although manufacturers are not required to use FR chemicals to meet flammability standards, FRs may be the most cost-effective means to meet a particular standard. Thus, staff's assessments of FR chemicals largely have been in support of staff's work toward flammability standards for consumer products, such as mattresses and upholstered furniture. In addressing flammability hazards, staff has made every effort to develop effective flammability standards that do not introduce additional hazards.

Children's Sleepwear

Staff's initial efforts focused on the use of FRs in children's sleepwear. Staff assessed the cancer risk from the OFR tris(2,3-dibromopropyl) phosphate (Tris or TDBPP), and the Commission subsequently banned the use of Tris in children's sleepwear.[5] Although the ban was later overturned in federal court for procedural reasons, many manufacturers stopped using FR chemicals in consumer apparel. In addition, the U.S. Environmental Protection Agency (EPA) issued a significant new use rule (SNUR) for Tris in 1987, which requires EPA to be notified before manufacture or importation of the chemical for a covered use; and it also obligates EPA to assess risks that may be associated with the use.[6]

In the late 1990s, for screening purposes, staff conducted an evaluation of FR use in children's sleepwear, including OFRs. Staff found that FRs were not widely used in children's sleepwear. Staff performed chemical migration studies on several sleepwear products treated with five different FRs, and completed risk assessments of these products. Staff concluded that, based on data available at the time, the evaluated products did not pose a hazard to consumers related to the FR use.

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[4] Although the current project is focused on organohalogen flame retardant chemicals, this section presents past CPSC staff work on a range of flame retardant chemicals, including inorganic and non-halogenated flame retardants, as well organohalogens.

[5] CPSC, 1977. Children's wearing apparel containing TRIS; interpretation as a banned hazardous substance. Federal Register 42, 18850-18854. [Later withdrawn following judicial proceedings.].

[6] EPA, 1987. 40 CFR § 721.6000. Available at: https://www.govinfo.gov/content/pkg/CFR-2013-title40-vol32/pdf/CFR-2013-title40-vol32-sec721-6005.pdf.

Upholstered Furniture Cover Fabrics

In the 1990s, as part of a CPSC regulatory proceeding to address the hazards of fires associated with upholstered furniture, staff proactively began evaluating the hazards of FR chemicals. Staff held a public meeting in 1998 to obtain information on chemicals that might be used to treat upholstered furniture cover fabrics. One result of the meeting was a prioritized list of candidate FR chemicals. Staff subsequently completed toxicity reviews for 16 high-priority classes of FR chemicals (more than 50 chemicals, including OFRs). These reviews contributed to a staff risk assessment and a National Research Council (NRC) report.[7] Six of the 16 high-priority classes were OFRs.

In 1999, Congress directed CPSC to arrange for an independent study by the NRC to conduct toxicological assessments for FR chemicals that are likely to be used as FRs for furniture upholstery. The NRC evaluated toxicological, epidemiological, and exposure data for the specified FR chemicals or classes of chemicals, and characterized risks to human health from exposure to furniture upholstery treated with such chemicals. The NRC concluded that eight of the 16 chemicals or classes could be used without presenting a risk to consumers, and recommended additional toxicity and exposure studies for the remaining eight FRs.[8]

CPSC staff also performed studies on the release of FRs from furniture fabrics and completed a risk assessment of eight FR chemicals that were most likely to be used in cover fabrics.[9] Staff concluded that five FR chemicals would not present a hazard to consumers, and additional toxicity and exposure data were needed on the remaining chemicals.

Upholstered Furniture Foam

To meet certain flammability standards, flexible polyurethane foams or other filling materials might be treated with FR chemicals. Until 2004, commercial mixtures containing the OFR pentabromodiphenyl ether (pentaBDE) and aromatic phosphate esters were the principal FR chemicals for flexible polyurethane foam. The sole remaining U.S. manufacturer of pentaBDE voluntarily ceased production in December 2004, due to concerns about environmental persistence and bioaccumulation. Other chemicals, in various chemical classes, have been used to replace pentaBDE, including the OFR tris(1,3-dichlropropyl-2) phosphate (TDCPP) and a commercial mixture containing the OFRs di(2-ethylhexyl) tetrabromophthalate and 2-ethylhexyl tetrabromobenzoate and the non-OFRs triphenyl phosphate and phenol isopropylated phosphate. In a peer-reviewed risk assessment,[10] staff concluded that melamine would not present a hazard to consumers, but that TDCPP might present a hazard, although additional exposure data were

[7] NRC, 2000. Toxicological Risks of Selected Flame Retardant Chemicals, National Research Council, National Academies Press, Washington, DC.
[8] NRC, 2000. Toxicological Risks of Selected Flame Retardant Chemicals, National Research Council, National Academies Press, Washington, DC.
[9] Babich, M.A., Thomas, T.A., 2001. CPSC staff exposure and risk assessment of flame retardant chemicals in residential upholstered furniture. U.S. Consumer Product Safety Commission.
[10] Babich, M.A., 2006. CPSC Staff Preliminary Risk Assessment of Flame Retardant (FR) Chemicals in Upholstered Furniture Foam. Tab B of Status Report: Peer Reviewed CPSC Staff Research Reports on Upholstered Furniture Flammability, December 2006. U.S. Consumer Product Safety Commission.

needed. Staff also concluded that additional toxicity data were needed before certain other FRs could be assessed.

Mattresses

Staff assessed several FR chemicals used in mattresses as part of development of CPSC's mattress flammability standards.[11] Staff concluded that chemicals, including ammonium polyphosphate, antimony trioxide, the OFR decabromodiphenyl oxide (DBDPO) (also called decaBDE), melamine, and boric acid would not present a hazard to consumers.

Other Assessments

In addition to the CPSC staff assessments discussed above, staff has sponsored work by a contractor, which resulted in several exposure assessments for selected individual flame retardant chemicals.[12] These reports, completed in 2015-2016, are available on CPSC's website.[13] Recently, staff completed preliminary risk assessments for two individual OFR chemicals (TDCPP, tetrabromobisphenol A (TBBPA)). These assessments were presented at the Society of Toxicology annual meetings in 2019[14] and 2020.[15]

Smoke Toxicity

Most fire deaths are due to smoke inhalation, rather than thermal burns. CPSC staff, in collaboration with NIST, conducted research on the smoke toxicity of home furnishings, primarily during the 1980s.[16,17,18] One of the goals of this work was to identify materials that, in a fire, produced smoke that was significantly more or less toxic than other materials. This would help manufacturers to develop safer products. This work also contributed to the development of computer simulations to evaluate the behavior of home furnishings in a fire.[19]

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[11] Thomas, T.A., Brundage, P., 2006. Quantitative assessment of potential health effects from the use of flame retardant (FR) chemicals in mattresses. U.S. Consumer Product Safety Commission.
[12] Tris(1,3-dichloro-2-propyl) phosphate (TDCPP); tris(chloropropyl) phosphate (TCPP); tris(2-chloroethyl) phosphate (TCEP); triethyl phosphate (TEP); triphenyl phosphate (TPP); 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB); di(2-ethylhexyl) tetrabromophthalate (TBPH); tetrabromobisphenol A (TBBPA); antimony trioxide (ATO).
[13] Available at: https://www.cpsc.gov/Research--Statistics/Technical-Reports.
[14] Babich M.A., Chen, X. 2019. Risk Assessment of the Flame Retardant Chemical Tris(1,3-Dichloro-2-Propyl) Phosphate (TDCPP). *The Toxicologist*, Supplement to *Toxicological Sciences*, 168(1), Abstract #1890. Available at https://www.toxicology.org/about/history/historical-documents.asp.
[15] Chen, X., Bevington, C., Harrad, S.J., and Babich, M.A. 2020. Risk Assessment of the Flame Retardant Chemical Tetrabromobisphenol A (TBBPA). *The Toxicologist*, Supplement to *Toxicological Sciences*, 174(1), Abstract #2220. Available at https://www.toxicology.org/about/history/historical-documents.asp.
[16] Gupta, K.C., 1987. Toxicity of combustion products from materials used in upholstered furniture evaluated separately and in combination. U.S. Consumer Product Safety Commission, Washington, DC. October 13, 1987.
[17] Orzel, R.A., 1993. Toxicological aspects of firesmoke: polymer pyrolysis and combustion. Occupational medicine (Philadelphia, Pa.) 8, 414-429.
[18] Thomas, T., White, S., Inkster, S., Babich, M., Neily, M., Lee, A., Saltzman, L., 2003. Estimation of low-level irritant and asphyxiant gas effects on egress time, Proceedings of the 14th Annual BCC Conference on Flame Retardancy, Stamford, CT.
[19] CPSC, 1990. CPSC HAZ-I. Fire Hazard Assessment Model. Consumer Product Safety Commission. September 29, 1990.

C) CPSC STAFF INTERAGENCY ACTIVITIES

Since 1998, in connection with CPSC staff work on upholstered furniture flammability, staff has collaborated with U.S. Environmental Protection Agency (EPA) staff on evaluation of FR chemicals. Staff worked with EPA to develop a draft SNUR in 2001, and in 2006, EPA issued a final SNUR for polybrominated diphenyl ethers (PBDEs), except decaBDE.[20]

Through an interagency agreement with CPSC, EPA's National Health and Environmental Effects Research Laboratory (NHEERL) studied the dermal absorption of selected FRs (decaBDE, TDCPP, and hexabromocyclododecane (HBCD)).[21,22] This work contributed to the CPSC staff risk assessments on upholstered furniture, mattresses, and infant sleepwear.

Furthermore, staff has participated with the EPA's Design for the Environment (DfE) alternatives assessment program to evaluate FR chemicals and substitutes for FR chemicals. This activity resulted in four EPA reports on flame retardants and FR alternatives in flexible polyurethane foam,[23] flame retardant alternatives to decaBDE,[24] flame retardants in printed circuit boards,[25] and flame retardant alternatives to HBCD.[26]

In 2005, CPSC staff nominated several FRs for toxicological testing by the National Toxicology Program (NTP) of the Department of Health and Human Services (HHS).[27] NTP published a final report on one FR chemical, antimony trioxide, in 2017.[28] CPSC staff presented a preliminary risk assessment using this NTP study at the Society of Toxicology annual meeting in 2019.[29] In June 2020, NTP published a prenatal development study of the OFR, tris(chloropropyl) phosphate (TCPP).[30] One (non OFR) FR chemical class, aromatic phosphates,

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[20] EPA, 2006. Certain polybrominated diphenylethers; significant new use rule. Federal Register 71, 34015-34021.
[21] Hughes, M.F., 2000. In vitro dermal absorption rate testing of flame retardant chemicals. National Health and Environmental Effects Research Laboratory, U.S. Environmental Protection Agency, Research Triangle Park, NC 27711. July 25, 2000.
[22] Hughes, M.F., Edwards, B.C., Mitchell, C.T., Bhooshan, B., 2001. In vitro dermal absorption of flame retardant chemicals. Food and Chemical Toxicology 39: 1263-1270.
[23] EPA, 2005. Furniture flame retardancy partnership: Environmental profiles of chemical flame-retardant alternatives for low-density polyurethane foam. Design for the Environment Program, U.S. Environmental Protection Agency, Washington, DC. September 2005.
[24] EPA, 2014. An alternatives assessment for the flame retardant decabromodiphenyl ether (DecaBDE). Final Report. Design for the Environment, U.S. Environmental Protection Agency. January 2014.
[25] EPA, 2015. Flame Retardants in Printed Circuit Boards. Final Report. Design for the Environment, U.S. Environmental Protection Agency. August 2015.
[26] EPA, 2014. Flame Retardant Alternatives for Hexabromocyclododecane (HBCD). Final Report. Design for the Environment, U.S. Environmental Protection Agency. June 2014.
[27] NTP, Nominated Substances, https://ntp.niehs.nih.gov/getinvolved/nominate/substances/index.html; Nomination Summary for Flame retardants (N20608) https://ntp.niehs.nih.gov/getinvolved/nominate/summary/nm-n20608.html
[28] NTP (2017) Toxicology and Carcinogenesis studies of Antimony Trioxide (CAS No. 1309-64-4) in Wistar Han [Crl:WI (Han] Rats and B6C3F1/N Mice (Inhalation Studies). NTP TR 590.National Toxicology Program, Research Triangle Park, NC 12209.
29 Chen X, Thomas TA, Cobb D, Babich MA (2019) Risk Assessment of the Flame-Retardant Chemical Antimony Trioxide (ATO). *The Toxicologist*, Supplement to *Toxicological Sciences*, 168(1), Abstract #2748. Available at: https://www.toxicology.org/about/history/historical-documents.asp.
[30] NTP (2020) Tris(chloropropyl) Phosphate (CASRN: 13674-84-5) in Sprague Dawley (Hsd:Sprague Dawley SD) Rats (Gavage Studies). NTP DART 01. National Toxicology Program, Research Triangle Park, NC 12209. Available at: https://ntp.niehs.nih.gov/go/dart01abs.

is currently undergoing testing. The staff also participated as members of the study design teams for the three chemicals.

In 2012, the staff nominated TDCPP for listing as "reasonably anticipated to be a human carcinogen" in the *Report on Carcinogens* (RoC). The RoC is a periodic report mandated by Congress and published by the Department of Health and Human Services that lists substances as being either "known" or "reasonably anticipated" to be carcinogens. The nomination is under review by NTP. In 2019, staff briefed the NTP Executive Board on the OFR project and the NASEM report.

CPSC staff has nominated certain FR chemicals of interest to EPA's Interagency Testing Committee (ITC). Through this process, EPA requests copies of certain unpublished health and safety information for specified chemicals from manufacturers (including importers). In 2020, staff requested that EPA include 30 OFRs (representing multiple subclasses recommended by the NASEM committee) in an upcoming EPA rulemaking seeking health and safety information. Previously, in 2012, at the request of staff, ITC added three FR chemicals to the Priority Testing List (TCPP, 2-ethylhexyl 2,3,4,5-tetrabromobenzoate (TBB), and di(2-ethylhexyl) tetrabromophthalate (TBPH)).[31]

D) Other Federal Agency Activities Related to Flame Retardant Chemicals

Other federal agencies have past or ongoing activities related to flame retardant chemical hazards and exposures. CPSC staff notes some of the most relevant work here.

In addition to the activities, mentioned above, which include interagency collaboration, EPA has evaluated a number of individual chemicals. For example, EPA's Integrated Risk Information System (IRIS) includes health hazard assessments for several FRs[32]; and recent work under the Toxic Substances Control Act (TSCA), as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act, includes FRs, including OFRs.[33] EPA is in the process of performing a risk assessment on HBCD[34]; and EPA recently identified TBBPA and tris(2-chloroethyl) phosphate (TCEP) as high-priority chemicals for upcoming risk assessments.[35]

Through the Tox21 program, a multi-federal agency collaborative, including EPA, NTP, the National Institutes of Health (NIH), National Center for Advances in Translational Science (NCATS), and the US Food and Drug Administration (FDA), many FR chemicals have been included in high throughput testing.[36,37]

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[31] EPA, 2012. Sixty-ninth report of the TSCA interagency testing committee to the administrator of the Environmental Protection Agency. Federal Register 77, 30856-30867.
[32] U.S. Environmental Protection Agency, Integrated Risk Information System, https://www.epa.gov/iris.
[33] U.S. Environmental Protection Agency, https://www.epa.gov/assessing-and-managing-chemicals-under-tsca.
[34] U.S. Environmental Protection Agency, Risk Evaluation for Cyclic Aliphatic Bromide Cluster (HBCD Cluster). https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/risk-evaluation-cyclic-aliphatic-bromide-cluster-hbcd. Accessed 4/2/20.
[35] U.S. Environmental Protection Agency, Chemical Substances Undergoing Prioritization: High-Priority. https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/chemical-substances-undergoing-prioritization-high. Accessed 4/2/20.
[36] Toxicology in the 21st Century (Tox21), https://tox21.gov/.
[37] See, for example, Tox21 Screening Library, https://comptox.epa.gov/dashboard/chemical_lists/tox21sl.

In addition to the work on FR chemicals nominated by CPSC, mentioned above, NTP has included FR chemicals in its testing program, employing the more traditional in vivo methods, as well as complementary animal models and in vitro methods.[38]

The Health Hazard Evaluation Program of the National Institute for Occupational Safety and Health (NIOSH) has assessed occupational exposures to FRs and other substances at facilities, including electronics recycling companies and gymnastics studios.[39]

The National Institute of Standards and Technology (NIST) has numerous projects and publications on properties, performance, mechanisms, and exposures for wide a range of flame retardant chemicals and materials.[40]

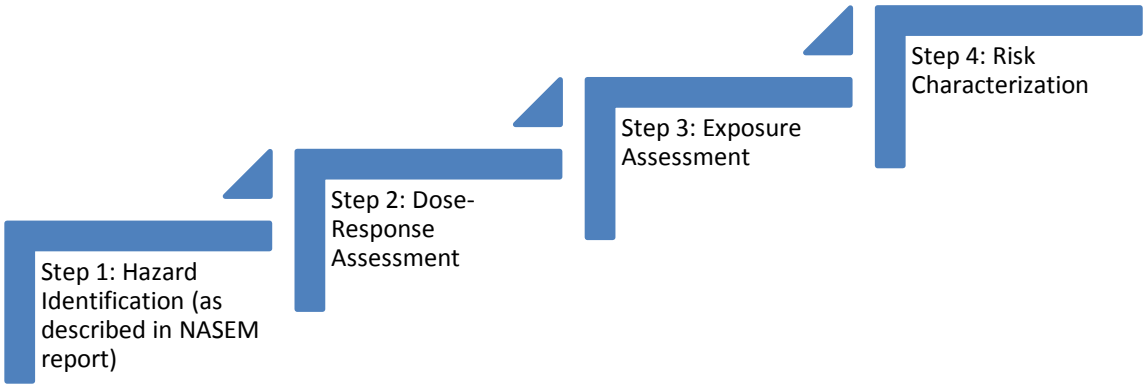
E) BACKGROUND ON CPSC RULEMAKING PROCESS CONSIDERING THE FHSA

CPSC's statutory framework directs rulemaking and other regulatory actions by the Commission. The FHSA is the main statute that provides for requirements related to chemicals in products. 15 U.S.C. §§ 1261–1278. The FHSA defines a "hazardous substance" as a substance or mixture that (*i*) is toxic, (*ii*) is corrosive, (*iii*) is an irritant, (*iv*) is a strong sensitizer, (*v*) is flammable or combustible, or (*vi*) generates pressure through decomposition, heat, or other means, if the substance "may cause substantial personal injury or substantial illness during or as a proximate result of any customary or reasonably foreseeable handling or use, including reasonably foreseeable ingestion by children." Therefore, CPSC staff assesses the human health risks associated with use of a product that contains the chemicals of interest. In other words, the FHSA is risk-based, reflecting consideration of exposure and risk, not simply presence of a toxic substance.

Figure 2 displays the general steps that CPSC staff uses in chronic hazard risk assessments that potentially could inform a CPSC rule. Step 1 is hazard identification and assessment of chemicals, such as described in the NASEM report. Hazard identification considers the evidence that the chemical(s) may cause a given adverse health effect in humans. In Step 2, staff would proceed to conducting dose-response analyses for the chemicals of interest. Dose response provides a measure of the chemical's potency. Conducting exposure assessments for chemicals from specified products is Step 3. The purpose of exposure assessment is to make quantitative estimates of exposure from specified consumer products. Step 4, risk characterization, is the qualitative and quantitative evaluation of the potential for adverse health effects associated with the products, based on the results of Steps 1–3. Each step requires specialized skills.

[38] See, for example, Nominated Substances, https://ntp.niehs.nih.gov/getinvolved/nominate/substances/index.html.
[39] NIOSH Health Hazard Evaluations (HHEs), https://www.cdc.gov/niosh/hhe/default.html.
[40] National Institute of Standards and Technology, https://www.nist.gov/.

Figure 2. General Risk Assessment Steps



Generally, a product or substance is considered "hazardous" if the exposure from reasonably foreseeable use (step 3) exceeds the acceptable daily intake (step 2).[41] A range of risk management options is available, if additional Commission action is needed to address a particular hazard. Options include voluntary standards, mandatory labeling, mandatory performance standards, recalls, bans, and information and education. Under the FHSA, the least burdensome option that adequately addresses the hazard at issue must be applied and the expected benefits of that action must bear a reasonable relationship to the costs.

Staff notes that CPSC statutes also provide the requirement for a CHAP. CPSC must convene a CHAP before proposing a regulation that would ban products based on a risk of cancer, birth defects, or gene mutations. This requirement comes from the Consumer Product Safety Act (CPSA) (15 U.S.C. §§ 2051–2089), and also applies to activities under the FHSA.

4. CPSC Staff's Plan for Class-Based Risk Assessment of OFRs

The process of completing a class-based risk assessment differs in several respects from a single chemical risk assessment.

1) Assessing multiple chemicals at one time requires cheminformatics and bioinformatics methods to group OFRs into classes based on chemical and biological similarity and to analyze large volumes of data.
2) The magnitude of the assessment requires explicit steps for project scoping and developing analysis plans.[42]
3) A class-based assessment focuses on health effects that are common to class members, similar to a mixtures or cumulative risk assessment. The common health effects within a class may not always be the most sensitive health endpoints for individual chemicals in the class.

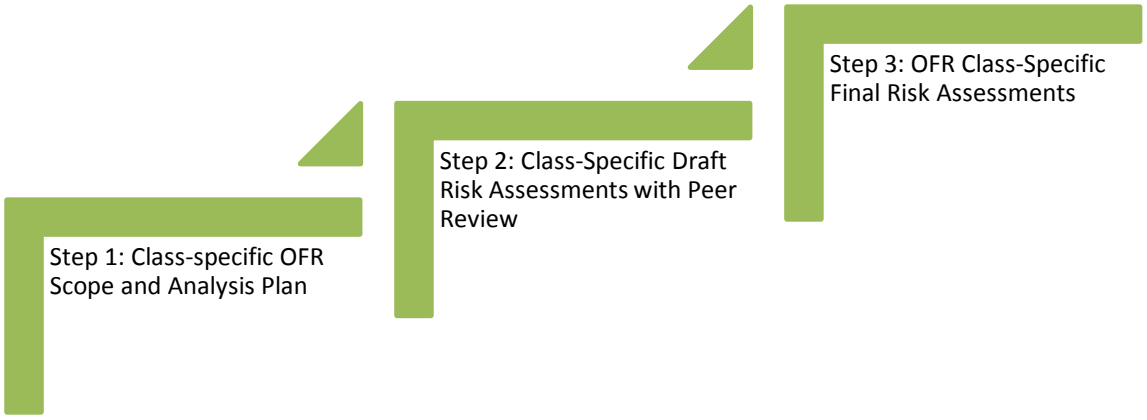
[41] CPSC (1992) Labeling requirements for art materials presenting chronic hazards; guidelines for determining chronic toxicity of products subject to the FHSA; supplementary definition of "toxic" under the Federal Hazardous Substances Act; final rules. Federal Register 57: 46626-46674.
[42] NAS (2009) Science and Decisions. The Silver Book. p. 67.

4) Most significantly, the class assessment necessitates the use of read-across methodology to fill data gaps, primarily for hazard identification, but also for dose-response assessment and exposure assessment.

A) Overview of the Class-Based Process

The class-based approach has three general steps: scoping document, draft risk assessment, and final risk assessment (Figure 3). The scoping document outlines the health endpoints, product types, and exposure scenarios for the draft risk assessment. Second, staff will conduct a draft risk assessment using the available data outlined in the scope document, as well as certain tools and methods to fill gaps in the available data. Following peer review, the draft risk assessment will be revised to produce the final risk assessment. After the final risk assessment is completed, staff will consider whether the risks are sufficient to recommend a rulemaking process. Note that each step in Figure 3 applies to all four risk assessment steps listed in Figure 2.

Figure 3. Class-Specific Risk Assessment Steps in Support of Regulation



CPSC staff plans to initiate work on multiple subclasses simultaneously. There are advantages to working on multiple scope documents early on, to assist in prioritizing the classes. However, due to the large number of classes, CPSC staff plans to stagger the completion of each class. Over time, and given the funding required, CPSC staff plans to start work on every class.

Step 1: Scope Document

Work on a class begins with the preparation of a scope document. The purpose of the scope document is to identify how much relevant data are available, what types of data (*e.g.*, hazard or exposure data) are available, and which of the product categories are relevant. A literature survey is used to develop a data evidence map, which identifies the amounts and types of hazard and exposure information are available. The data map helps to identify the health effects of interest, as well as the relevant product types and exposure pathways. Staff recommends using a contractor to identify available product use information for the OFR class as part of the scope

document. This information is used to create a conceptual exposure model, which identifies likely sources, pathways, receptors, and effects. The scope document also includes a literature search plan that shows where and how CPSC staff will look for data to inform its risk assessment. The scope document shows how CPSC staff will focus its efforts for risk assessment. For example, toxicological endpoints of interest and likely exposure pathways will differ from class to class.

Scope documents synthesize readily available information, such as information found in completed assessments, database sources, and targeted literature reviews. The scope document uses results of a literature survey to present potential hazards and exposures for chemicals within a class, and provides an analysis plan. Additional details for these technical support activities are included in Tab C.

Staff recommends that the Commission publish a scope document to start the risk assessment for each class, given the expected complexity of a class-based risk assessment. Scope documents provide a mechanism to show how one class-based assessment will differ from another, determine data availability, and obtain public feedback.

Following completion of a scope document, CPSC staff will determine whether there is sufficient information available, as a class, to conduct a class-based risk assessment. This determination will be based on available data, as well as the availability of technical approaches that can be used for filling data gaps.

Staff plans to consider a number of factors to prioritize work on the subclasses as scope documents are completed. Because of the challenges inherent in managing the complex set of activities required to complete multiple risk assessments, as well as resource limitations at any given point in time, staff will prioritize starting work on subclasses, based on availability of hazard and exposure data, an initial assessment of data concordance, and other readily available information, such as completed assessments for a subclass, or for multiple subclass members.

Step 2: Draft Risk Assessment

Step 2 is to perform a draft risk assessment using the available data. CPSC staff plans to follow established risk assessment guidelines, including the CPSC Chronic Hazard Guidelines.[43] CPSC staff plans to adapt these guidelines, as appropriate, for use in class-based, rather than single-chemical risk assessments. Risk assessment includes four steps: (*i*) hazard identification; (*ii*) dose response analysis; (*iii*) exposure assessment; and (*iv*) risk characterization.[44] Risk characterization cannot be completed until all previous steps have been completed. In the class approach, compared to single chemical evaluation, each of the four steps becomes more complicated. The assessment begins with a detailed literature search that focuses on the health endpoints and exposure pathways identified in the scoping process. If necessary, certain tools and methods, such as read-across approaches, may be used to fill data gaps identified in the first three steps. The possibility of interactions between different chemicals in a class may also be

[43] CPSC (1992) Labeling requirements for art materials presenting chronic hazards; guidelines for determining chronic toxicity of products subject to the FHSA; supplementary definition of "toxic" under the Federal Hazardous Substances Act; final rules. Federal Register 57: 46626-46674. Available at: https://www.cpsc.gov/s3fs-public/pdfs/blk_pdf_chronichazardguidelines.pdf.

[44] National Research Council 1983. Risk Assessment in the Federal Government: Managing the Process. Washington, DC: The National Academies Press. https://doi.org/10.17226/366. Available at: http://nap.edu/366.

considered in hazard identification and dose-response steps, while aggregate and cumulative exposure may be considered in exposure assessment. Risk characterization must be expanded to include all the chemicals in the class, and may include cumulative risk as well.

CPSC staff will use the results of the literature survey to complete a class-specific literature search. This literature search will identify and screen relevant information that can be used to support class-based risk assessments. CPSC staff plans to consider empirical data, as well as other types of information, such as computer-based and modeling methods (*e.g.*, read-across, structure-activity relationships, toxicokinetic modeling, and exposure modeling) for both toxicology and exposure information to fill data gaps for data-poor chemicals within a subclass.

Read-across is a complex process in itself. In a read-across approach, the chemical or biological properties of the data-rich members of a class (anchors) are used to interpolate or extrapolate to the properties of the data-poor members (targets). The exact method used may vary from class to class. Potential methods include, for example, quantitative structure activity relationships (QSARs), analysis of the mode of action (MOA) or adverse outcome pathway (AOP), or the use of new alternative methods (NAMs). Read-across generally includes an uncertainty assessment, and requires evidence-based justification.

As with any risk assessment, the draft risk assessment includes a qualitative or quantitative assessment of uncertainty in each step of the risk assessment. In addition, any uncertainties associated with the class-based approach, such as read-across, must also be included.

During the risk assessment process, CPSC staff may find that additional information is needed to inform risk assessment efforts for certain class members. In this case, if sufficient information is not available, CPSC staff would develop recommendations to defer action or pursue additional information-gathering activities, such as exposure studies or nomination to NTP or ITC for toxicity testing.

The completed draft risk assessment will be submitted for peer review in accordance with the requirement for peer of review of "influential" documents and accepted scientific practice.

Step 3: Final Risk Assessment

Finalizing the risk assessment includes submitting the draft risk assessment to peer review, and revising the document in response to peer reviewers' comments. The final risk assessment includes an overall assessment of the risks posed by the class and the need for risk management activities.

CPSC staff plans to complete a one-time update of the literature search after the draft assessment because new data may become available. CPSC staff plans to consider this information, along with peer review and public comments before finalizing the risk assessment. CPSC staff plans to use available empirical data and notes that new empirical data can influence modeled estimates when considering a class-based approach.

Following completion of the final risk assessment, CPSC staff, in consultation with senior management, will need to determine whether there are risks present that warrant Commission action to mitigate. There are several possible outcomes:

- If the class is found to present a hazard to consumers, the Commission may direct the staff to convene a CHAP as a prelude to rulemaking.

- If the draft risk assessments suggests that the class presents a hazard to consumers, but the uncertainty is high, staff could either: (a) obtain additional data to refine the draft risk assessment, or (b) defer action and work on other classes.
- If the draft risk assessment does not suggest a hazard to consumers, the staff may simply move on to the next class.

Next Steps

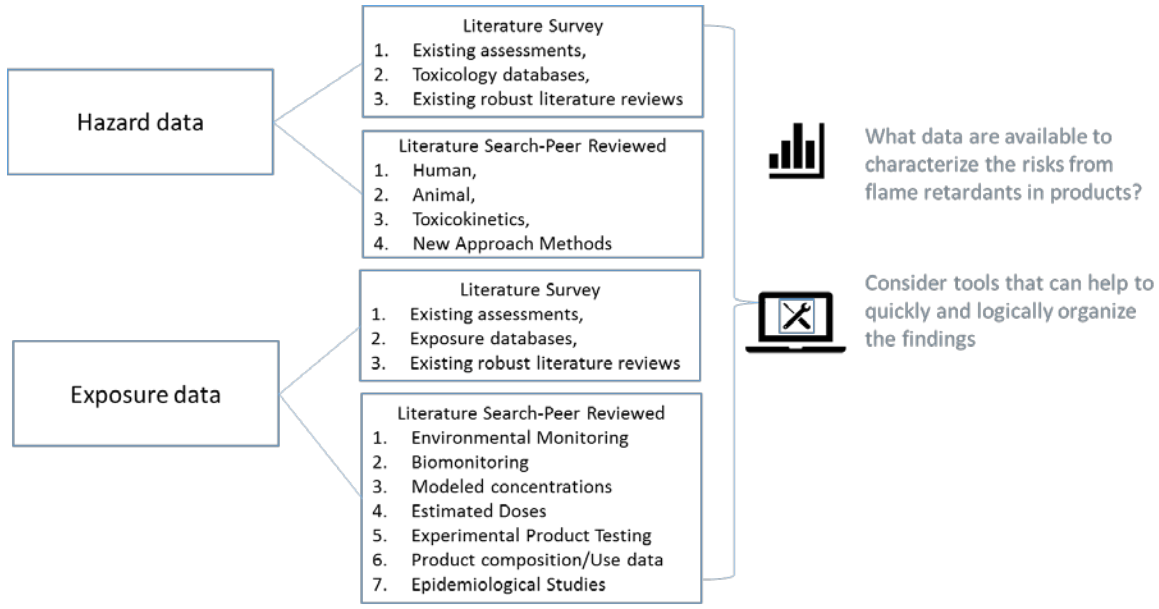
If the final risk assessments suggest the need for regulatory intervention for an OFR class, the Commission may proceed with established rulemaking procedures. The rulemaking process may require the Commission to convene a CHAP, if the hazard(s) presented by the class include carcinogenicity, mutagenicity, or developmental effects. The Commission could also choose to convene a CHAP for other hazard types. Following a CHAP, the staff will assemble the documents needed to issue a notice of proposed rulemaking (NPR), including the final risk assessment, economic analysis, and draft proposed regulation. If the Commission publishes the NPR, the staff must respond to public comments and revise the proposed rule, as appropriate, before presenting a draft final rule (FR) to the Commission.

B) THE RISK ASSESSMENT PROCESS

Risk assessment comprises four steps: (1) hazard identification, (2) dose-response assessment, (3) exposure assessment, and (4) risk characterization (Figure 2). Risk assessments, whether for single chemicals or classes, vary in their scope and complexity. They are fit-for-purpose, based on the needs of the organization.[45] Risk assessment is an iterative process. Staff expects that class-based risk assessments also can vary in scope and complexity, but notes that increased complexity is a central consideration, given that class-based assessments require simultaneous characterization of multiple class-members. Class-based risk assessments necessitate a trade-off between coverage of multiple chemicals and the level of detail presented for each chemical. The degree of refinement of hazard, exposure, and risk information and analysis for class-based risk assessments must be sufficient to support decision making within CPSC's rulemaking process. Figure 4 provides an overview of the process CPSC plans to use to identify and assess hazard and exposure information that can be used for class-based risk characterization.

[45] Fit-for-purpose generally refers to processes that produce needed outputs and outcomes. It indicates that processes must have flexibility and allow adjustments, based on identified needs. It also implies that processes must work within established frameworks, such as federal statutes, as well as within the reality of available resources.

Figure 4: Overview of Process Used to Identify Hazard and Exposure Data for Use in Class-Based Risk Assessment



Source: Adapted from a presentation by Cara Henning, Kevin Hobbie, and Ashley Williams, ICF International Inc., to CPSC staff. CPSC public meeting, 30 April 2020.

Hazard identification is the qualitative characterization of toxic effects of chemicals, while dose-response assessment is the quantitative characterization of the relationship between doses or exposure and the occurrence of toxic effects in exposed laboratory animals or human populations.

CPSC staff plans to follow these general steps when completing class-based hazard and dose-response assessments for use in class-based risk assessment:

1) Conduct literature survey to identify readily available toxicity information from databases and completed assessments to determine extent, range, and nature of toxicity data and inform development of PECO[46] statement (Scope document);
2) Integrate information within the scope document to create an analysis plan and identify toxicity end points to be evaluated (Scope document);
3) Perform literature search to identify additional hazard information, including quantitative dose-response data (Draft Risk Assessment);
4) Evaluate and integrate hazard information, select studies for derivation of toxicity values, derive toxicity values (Draft and Final Risk Assessments); and

[46] PECO refers to population (P), exposure (E), comparator (C), and outcomes (O) of interest.

5) Iterate, as needed, refine quantitative dose-response analyses, apply science and policy decisions for subclasses for use toxicity values in risk assessment (Draft and Final Risk Assessment).

These steps are discussed in more detail in Tab A.

Exposure assessment quantitatively characterizes the extent of human exposures in identified scenarios or situations. Exposure assessment is the process of estimating or measuring the magnitude, frequency, and duration of exposures, and the size and characteristics for the exposed population.[47,48]

CPSC staff plans to follow these general steps when completing class-based exposure assessments for use in class-based risk assessments:

1) Identify sources (uses) of OFRs through market-use profiles, and identify relevant physicochemical properties of chemicals. (Scope document)
2) Identify readily available exposure information from databases and completed assessments to inform development of PECO statement and likely exposure scenarios. (Scope document)
3) Integrate information within the scope document to create a conceptual model to visualize exposure sources, pathways, and receptors. CPSC staff plans to characterize exposures from all sources, including consumer products. (Scope document)
4) Identify additional exposure information through literature searching and screening. (Draft Risk Assessment)
5) Evaluate and integrate exposure information. Where appropriate, CPSC staff will estimate aggregate and cumulative exposures. (Draft and Final Risk Assessments)
6) Iterate, as needed, and quantify exposure scenarios for use in Risk Assessment. (Draft and Final Risk Assessment)

These steps are discussed in more detail in Tab B.

Risk characterization is the part of a risk assessment that estimates the potential occurrence of health effects under specified conditions of exposure. It may include characterization of affected populations, as well as characterization of uncertainties and variability. CPSC staff generally characterizes non-cancer risks using a hazard index approach.[49] A hazard index greater than one is considered to indicate a potential risk of adverse health effects. In contrast, for evaluation of cancer risks, an individual lifetime excess risk great than one per million is the default level of concern, which may trigger labeling or other action.[50] An important part of risk characterization is to describe the variability, uncertainty, and limitations of the risk assessment.

[47] Ibid., CPSC 1992.
[48] EPA 2019. Guidelines for Human Exposure Assessment. Available at: https://www.epa.gov/sites/production/files/2020-01/documents/guidelines_for_human_exposure_assessment_final2019.pdf.
[49] Ibid., CPSC 1992.
[50] The Commission determines on a case-by-case basis whether action is needed to reduce a hazard.

A class-based assessment requires descriptions of all assumptions or methodologies used for the class approach.

Another consideration of class-based risk assessment is the possibility of interactions when individuals are simultaneously exposed to members of the same class. If class members act by a similar mode of action, or have a common health endpoint, it is reasonable to consider whether there are additive, synergistic, or antagonistic effects, such as with phthalates.[51] Staff will evaluate the potential for mixture or cumulative effects following established guidelines.[52,53,54]

Risk assessment is also an iterative process. Therefore, work in each step of a risk assessment generally can be conducted in a tiered manner, where the tiers require increasingly complete, detailed, and quantitative data for a chemical, or across a group or subclass of chemicals. The level of refinement in assessments is related to data availability. Assessments can be iterative to incorporate new data and more involved analyses. Tiering is discussed in more detail in Tab C. Tab C also provides a description of different technical support activities needed to support class-based risk assessment. The scope of the technical support activities required for each class will vary, based on the magnitude and diversity of available hazard and exposure data.

5. Staff Recommendations

Staff recommends undertaking class-based risk assessments of OFRs in selected types of products by proceeding with several activities. These foundational activities, performed by CPSC staff, will set up and support the overall project as it proceeds through the risk assessment process and through time. Some of the recommendations are cross-cutting for both the OFR subclasses and the major parts of a chemical risk assessment. These activities will help provide an organization framework for the project and build efficiencies. In Section 6 below, staff recommends additional specific tasks in fiscal year 2021, to begin the risk assessment process for specified OFR subclasses with work largely to be performed by contractors.

1. Develop and maintain a list of OFR chemicals. Adopt the class-based approach using the 14 subclasses, acknowledging that the number of OFR chemicals within each subclass can be refined as new OFR chemicals are identified. Update and maintain NASEM OFR class lists, and associated analog substances, and recommend to EPA to include these chemical lists on EPA's CompTox Chemicals Dashboard.[55] The Dashboard already contains records for many OFRs that provide access to a wide variety of chemical and biological data.

[51] Chronic Hazard Advisory Panel (CHAP) (2014) Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives. U.S. Consumer Product Safety Commission, Bethesda, MD. July 2014. http://www.cpsc.gov/chap.

[52] EPA (2000) Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC 20460. August 2000. EPA/630/R-00/002. http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4486

[53] ATSDR (2004) Guidance Manual for the Assessment of Joint Toxic Action of Chemical Mixtures. May 2004. In: U.S. Department of Health and Human Services PHS, Agency for Toxic Substances and Disease Registry, Division of Toxicology (ed). U.S. Department of Health and Human Services, Atlanta, GA.

[54] NRC (2008) Phthalates and Cumulative Risk Assessment. The Task Ahead. Committee on the Health Risks of Phthalates, National Research Council, National Academy Press, Washington, DC.

[55] https://www.epa.gov/chemical-research/comptox-chemicals-dashboard.

2. Initiate a scope document for each OFR class. Determine whether there is sufficient information available, as a class, to conduct a class-based risk assessment, based on available data, as well as the availability of technical approaches that can be used for filling data gaps. Open a docket related to each OFR class when the scope document is complete, and invite stakeholders to provide information and comment to CPSC during specified public comment periods.
3. Use a combination of approaches to proceed on multiple activities related to scoping and completing class-based risk assessments. Following publication of an updated OFR chemical list, CPSC staff recommends initiating work on multiple scope documents. Following publication of scope documents, CPSC staff recommends initiating work on some class-based risk assessments. CPSC staff recommends identifying data needs and pursuing generation of new toxicity and/or exposure data following completion of scope documents. These different technical support activities can be worked on in parallel. Initially, CPSC staff recommends investing a majority of time and resources in scoping. Over time, CPSC staff recommends shifting this focus from scoping. This shift will move toward completion of risk assessments, generation of new data, or other action, as informed by available information and science policy decisions.
4. Consider the use of NAM data as an approach to estimate toxicity. For example, in the absence of sufficient toxicity information on some members of a class, NAM data, in conjunction with human or animal toxicity data for other class members or close analogs, could help in reaching science-based conclusions for a class. When no human, animal, or NAM data are available for any class member or close analog, staff recommends generating new toxicity data, using either traditional methods or NAMs, as appropriate.
5. Develop and maintain a set of procedures and best-practices for identifying, searching, and extracting data from toxicity and exposure databases to inform literature surveys. This set of procedures will apply to any OFR subclass, and is needed because available databases change over time. Develop and maintain toxicity and exposure seed data sources to inform literature searching. This set of seed articles will apply to any OFR subclass, and is needed because use of seed articles is an accepted and efficient way to quickly identify and screen relevant data sources for a specific OFR subclass. Develop and maintain a set of criteria for acceptable tools to identify, screen, evaluate, extract, and integrate data for use in class-based risk assessment.
6. During scoping, identify all uses of OFR chemicals to determine which OFRs are used or have been recently used in consumer products, which OFRs have industrial or commercial applications only, and which OFRs have been phased out of use. This scoping will also inform how current uses of OFR chemicals compare with the product categories in the petition. Some classes may have more narrow applications (one or two of petitioned uses), while other classes may have broader applications. Understanding the market profile, uses, and trends of OFRs is an important part of characterizing exposure and risks. This scoping can inform which classes CPSC staff prioritizes for risk assessment. Based on this scoping, it is possible that some OFR classes could be addressed through alternative risk management and need not proceed through all CPSC risk assessment and management steps. For example, CPSC staff could publish a list of OFR chemicals that do not appear to be manufactured, formulated into consumer products or building materials, or recycled into

product content following completion of market research and finalization of a scope document, and could request public comment or refer the list to EPA for surveillance.

7. Update this project plan to reflect lessons learned, over time, from completion of scoping and risk assessment activities. In the update, CPSC staff will present science-policy recommendations, such as for decisions related to the use of NAM data in hazard assessments under the FHSA.

6. Specific Recommended Activities for Fiscal Year 2021

Staff has identified several options for activities in fiscal year 2021. Staff has grouped these possible activities into two main options. Option A is work performed by contractors, as directed and monitored by CPSC staff, and Option B is a NASEM committee project. These two options are discussed separately below. Staff notes pros and cons of choosing one of these two main options, and for proceeding with one or more of the activities in the contractor/CPSC staff option.

For fiscal year 2021, CPSC requested a recurring $1.5 million above baseline appropriations in the Performance Budget Request, as existing baseline appropriations are insufficient to complete this work. Thus, planned work identified below is contingent upon receiving this additional appropriation and additional appropriations in future years to continue the work.

As part of the CPSC-sponsored NASEM project, NASEM staff provided an outline of a possible NASEM project to perform hazard assessments only, for the chemical classes identified in the NASEM 2019 report.[56] NASEM staff estimated that the cost for NASEM to complete hazard assessments for 10 of the 14 subclasses is approximately $13 million, including $1.5 million for a pilot project for one class. NASEM staff indicated that available data are likely insufficient for the remaining four subclasses. Staff notes that the NASEM estimate does not include the other risk assessment steps (*i.e.*, dose-response and exposure assessment). This work would require funding beyond the estimated cost for the hazard assessments. The entire project (all OFR subclasses with sufficient data, and all analyses required to complete risk assessments) will require multiple years to complete.

Each of the two main options would be supported by the $1.5 million above baseline appropriations in the Performance Budget Request. NASEM staff estimated that the initial pilot phase for a NASEM project would cost about $1.5 million. CPSC staff estimates that the group of activities that would be performed by contractors, directed and monitored by CPSC staff, together would cost about $1.5 million.

Staff recommends proceeding with Option A, which is the group of activities largely to be performed by contractors, directed by CPSC staff. Some work may also be performed through coordination between CPSC staff and staff at other federal agencies, such as EPA or NTP, for chemicals of common interest. Depending on resource availability, some of the recommended work by contractors could also be performed by CPSC staff.

[56] Letter from Gregory H. Symmes, Executive Director, Division of Earth and Life Studies, The National Academies of Sciences, Engineering, and Medicine, to Kristina Hatlelid, U.S. Consumer Product Safety Commission. April 4, 2019.

The pros and cons for the recommended Option A activities performed by contractors, directed by CPSC staff, are below.

Pro: Work on activities that support development of scope documents for each class is critical because it will help define relevant available information and how CPSC staff will proceed with risk assessment for each class.

Pro: Work by contractors can be more nimble in iterative decision-making that may be needed during the process. For example, as issues with data availability, quality, or other obstacles are identified, staff, in consultation with CPSC management, and following federal procurement rules, can respond and make adjustments. (The NASEM process, by design, does not allow for frequent interactions between CPSC staff and committee.)

Pro: Selecting experienced contractors provides technical proficiency and efficiency.

Pro: Staff can initiate concurrent contract work on multiple interrelated parts of the risk assessment process (*e.g.*, both hazard assessment and exposure assessment activities).

Pro: May require, overall, less funding for the hazard assessment tasks.

Con: Requires resources to be available for contractors.

Con: Staff would not have the benefit of the experience and advice in the initial stages of the class-based hazard assessment that would be provided by the expertise of a NASEM study; this can be mitigated through contractor support.

Although Option B, a NASEM committee study, would come with numerous benefits, it would also likely be relatively time- and resource-consuming, which would result in limited resources for concurrent work on other portions of the project. If the Option B NASEM study is selected to proceed, staff recommends that CPSC staff develops the scope documents and proceeds with the exposure assessment options.

A) Option for Work to be Completed by Contractor under Staff Direction

In fiscal year 2021, staff will initiate project work on assessing the risks associated with OFRs in specified products, if funding is authorized, and staff resources are made available. Staff anticipates that several specific activities of the project will involve work performed by contractors, directed and monitored by CPSC staff. Some of this work may also be performed through collaboration and agreements with other federal agencies.

Although the overall process of risk assessment includes some steps that will be completed sequentially, staff has identified activities that can be initiated and proceed in parallel. Staff expects to begin with developing scope documents for each class, by conducting OFR market and use research, and completing literature surveys to identify and collect data and other information within the two general categories of hazard and exposure. Based on an evaluation of available information, staff will identify and specify subsequent analysis tasks. Specific activities are described below.

1) Initial Scoping and Scale-Up

Staff recommends completing literature surveys and scope documents for one or two chemical subclasses. Staff proposes to proceed with this work through a contract or interagency

agreement. This activity supports Step 1, Scope Document, of the class-based risk assessment process in Part 4 of this report.

Hazard assessment for OFRs includes defining the complex series of activities that will lead to identification and evaluation of data that can be used to understand the hazards of each class. The NASEM committee recommended, as a first step, to complete class-specific literature surveys. These surveys are then used to develop scope documents for the class-based risk assessments.

Many data and information sources contain both hazard and exposure data. One coordinated effort to survey all potentially relevant information allows hazard and exposure information to be collected and considered efficiently.

The scope documents will describe available data, such as from bibliographic databases, other databases that compile data, and other information from a variety of sources, and completed assessments. These documents will include information developed in other activities, such as the market and use research described in Activity 3 below. The work will also describe methods, tools, and opportunities for automation of the process of identifying, screening, extracting, evaluating, and integrating data to complete hazard assessments for specific toxicological endpoints, and to complete exposure assessments for specific products and product classes.

The completed literature surveys and documents will demonstrate how staff will proceed with the class assessments. Completion of these initial one or two class-based literature surveys and scope documents will allow staff to move to the next phase of the assessment process for OFR classes, as well as to evaluate the survey and scope development process and make adjustments to improve efficiency for the remaining classes. Furthermore, scope documents help to prioritize classes, by identifying the more data-rich and data-poor classes. Depending on the timing of funding, the initial scoping, initiated in FY 2021, will take about 1 year to complete.

2) Scope Document Development

If the initial scoping project for two subclasses is completed in FY 2021, staff recommends initiating work towards completing the literature surveys and scope documents for the remaining chemical subclasses. Staff proposes to proceed with this work through a contract or interagency agreement. If initiated in FY 2021, scope document development for all classes will take about 2 years complete; individual scope documents will take about 6 months each to complete. With a staggered start schedule, subclass scope documents will be completed in a staggered fashion. This activity supports Step 1, Scope Document, of the class-based risk assessment process in Part 4 of this report.

3) OFR Market and Use Research

Staff recommends identifying use information for OFR chemicals. This information will be included in scope documents. Given that this work will provide the foundation for other activities in this project, staff recommends proceeding with research for at least two subclasses, or more, if resources allow. Staff proposes that this work be done through a contract. This activity supports Step 1 of the class-based risk assessment process in Part 4 of this report.

This activity would need to begin as soon as possible, because it contributes to scope document development and analysis plans.

This project would identify uses of OFR chemicals within each subclass through development of a market-use profile. Each market-use profile will provide an overview of known and potential uses, based on market reports, sector-specific databases, and product surveillance. The project would identify OFRs that are used, have recently been used, or could potentially be used in consumer products, OFRs that have industrial or commercial applications only, and OFRs that have been phased out of use for many years. Although all uses will be researched, the market use profile will focus on identifying types of consumer products containing OFRs. This project, if initiated in FY 2021, will take about 1 year to complete.

4) Expedited Scope Document Development to Support Hazard and Exposure Assessment Activity

For class-based assessments, the general steps in the process for each class include a literature survey and other information collection and development of a scope document (Step 1 in the process to complete class-specific scope documents), followed by a more detailed, in-depth literature search to identify specific relevant data, and screening, extracting, and evaluating the data for use in a hazard assessment (initiation of Step 2, draft risk assessment). This activity supports Step 1, Scope Document, of the class-based risk assessment process in Part 4 of this report.

Although staff anticipates that literature searching and related work will be performed by contractors, a literature search contract project in FY 2021 must be preceded by a literature survey and scope document. Staff recommends that CPSC staff initiate an expedited literature survey and scope document development for a class and its analogs. This expedited scope document would define and support the literature search contract options proposed below (either a CPSC contract, or a NASEM committee). Staff proposes to focus on one or two data-rich OFR classes that are likely to be better characterized from the start, such as a class that contains relatively well-known chemicals, or that has several chemicals or groups of chemicals that have already been reviewed or assessed by other organizations, including EPA, NTP, Health Canada, or the European Chemicals Agency (ECHA).

CPSC staff's goal is to develop scope documents for all 14 OFR subclasses in the early part of the project, given that a completed scope document is needed before proceeding to the second step of the process. However, the reality of time and resource constraints, in conjunction with a preference to proceed and devote resources to the next steps as quickly as possible, may necessitate that the scope documents will not all be completed at the same time.

To the extent that most or many of the scope documents for the 14 subclasses can be completed and considered together, staff will perform a prioritization exercise to choose the order that subclass literature searches and analyses will be conducted.

CPSC staff plans to maintain a set of best practices related to processes used to complete class-based hazard assessment. These best practices will inform work on future classes. CPSC staff recommends maintaining and updating these best practices as a separate guidance document.

This activity, if initiated in FY 2021, will be completed in FY 2021, if possible, to support proceeding with the next step (literature search) as part of the FY 2021 work.

5) Hazard Identification and Exposure Assessment Literature Search

Based on the expedited literature surveys and scope documents for two classes (Activity 4), this project would proceed with the next step in the process. This activity encompasses the detailed literature search to identify relevant hazard data for specific toxicological endpoints, and screening, extracting, and evaluating the data for use in a hazard assessment. This project also encompasses the detailed literature search to identify relevant exposure data for specific exposure scenarios identified in the scope document, and screening, extracting, and evaluating the data for use in exposure assessment. This activity supports Step 2, Draft Risk Assessment, of the class-based risk assessment process in Part 4 of this report.

Staff recommends proceeding with a hazard and exposure assessment literature search for up to two specified OFR classes. This project would proceed through a support contract, such as a task order under an existing CPSC contract for toxicology services. Hazard and exposure assessment are distinct, but interrelated. Many scientific articles contain both hazard and exposure data. One coordinated effort to identify all potentially relevant information allows hazard and exposure information to be screened efficiently. If initiated in FY 2021, this project will take about 2 years to complete.

6) Exposure Assessment

CPSC staff plans to complete a conceptual model, that is, develop qualitative exposure scenarios informed by literature surveys of exposure-data, including product uses for OFRs, for one or two subclasses, as identified in Activity 4 above. The results of the literature survey, the exposure conceptual model, and the market and use research are part of a completed scope document that can be used to inform the more detailed literature search of OFR chemicals.

CPSC staff plans to maintain a set of best practices related to processes used to complete class-based exposure assessments. These best practices will inform work on future classes. CPSC staff recommends maintaining and updating these best practices as a separate guidance document. This project will take about 6 months to complete. This activity supports Step 1, Scope Document, of the class-based risk assessment process in Part 4 of this report.

7) Product Exposure Testing Plan

Staff recommends exposure evaluation through use of existing or de-novo testing of OFR-containing products and materials, whenever possible. Staff proposes developing a product testing plan to tailor generation of new product exposure testing data based on whatever existing data are available. The plan will compile available testing methods and approaches used by CPSC and other organization for exposure testing. After FY 2021, and following scope document development, CPSC staff recommends initiating exposure testing through a contract or interagency agreement. This activity supports Step 2, Draft Risk Assessment, of the class-based risk assessment process in Part 4 of this report.

The resulting project would contract with an organization, such as an academic or government laboratory, capable of detecting and analyzing a wide range of OFR chemicals in a

variety of consumer products. The laboratory should have experience with determining OFR concentrations in consumer products or materials, as well as experience with migration and emission testing of products using standard methods. A laboratory that has available samples containing known amounts of OFRs, *e.g.*, because of the laboratory's other studies on such products or materials, is well suited to completing this exposure testing.

Staff is aware of a few laboratories that are capable of completing this work. Laboratories that are already analyzing OFR chemistries and products similar to CPSC's interests are uniquely suited to assist staff by completing additional exposure testing that is fit-for-purpose for CPSC staff's needs. A wide range of tests can be completed to answer questions about how OFR chemicals migrate into biological fluids or matrices in contact with the human body. Readily available emissions tests can inform how OFR chemicals are emitted from materials and transported into surrounding indoor air and dust.

Results of exposure testing will be used to estimate consumers' direct exposures to chemicals from use of, or proximity to, consumer products that contain such chemicals.

This planning project, if initiated in FY 2021, will take about 6 months to complete. The resulting plan would inform exposure assessment work to be performed in FY 2022 and future years, as needed.

B) OPTION FOR NASEM STUDY: HAZARD ASSESSMENT IN SUPPORT OF CLASS RISK ASSESSMENT (PILOT)

As part of the CPSC-sponsored project with NASEM, NASEM staff provided an outline of a possible NASEM project to perform hazard assessments for chemical classes identified in the NASEM 2019 report.[57]

NASEM staff assumed that data exist for 10 of the 14 classes identified in the report to reach a decision of "potentially hazardous," "not hazardous," or "discordant data." NASEM proposed a pilot assessment of one chemical class. The assessments of the remaining nine classes would be carried out in a phased approach following the pilot.

In the pilot phase, a NASEM committee would illustrate specifically how each step of the hazard assessment should be conducted, and would develop guidelines for data analysis and integration. As part of the resource estimates, NASEM assumed that the committee would conduct systematic reviews and consider three health end points to investigate hazard. NASEM estimated that a committee would include 14 experts, and that five key NASEM staff would assist the committee. NASEM provided an approximate cost estimate and proposed that the project would require 24 months to complete.

For the remaining nine chemical classes with existing data, NASEM staff proposed that three studies (one chemical subclass each) could be conducted in parallel. Each study would include a committee of 14 experts, assisted by five NASEM staff, and would require 18 months to complete (4.5 years in total for nine subclasses).

[57] Letter from Gregory H. Symmes, Executive Director, Division of Earth and Life Studies, The National Academies of Sciences, Engineering, and Medicine, to Kristina Hatlelid, U.S. Consumer Product Safety Commission. April 4, 2019.

The NASEM costs and time estimates for 10 classes were informed by assumptions made regarding how to identify, evaluate, and integrate hazard data. These estimates likely would be refined after completion of pilot work. NASEM staff emphasized that the resource estimates do not include the costs of toxicology tests that may be needed to fill data gaps and resolve discordant data.

CPSC staff notes that the NASEM proposal covers only hazard assessment. CPSC staff or contractors also would have to conduct dose-response analyses and exposure assessments for each chemical class, to complete risk assessments of products-containing OFRs.

Pros and cons of selecting this activity for FY 2021:

Pro: NASEM is a private, non-profit society of distinguished scholars. Established by an Act of Congress, NASEM is charged with providing independent, objective advice to the nation on matters related to science and technology. Scientists are elected by their peers to membership in the Academies for outstanding contributions to research. NASEM is committed to furthering science in America, and its members are active contributors to the international scientific community. NASEM is recognized for its capabilities to supply services for establishing balanced committees of scientists recognized as national and international experts. NASEM committee consensus reports are accepted nationally and internationally as comprehensive, high-quality scientific technical scientific reports, which can be relied on as independent, objective, and nonpartisan advice for use by regulatory agencies in support of risk management decisions.

Pro: Having completed the study, "A Class Approach to Hazard Assessment of Organohalogen Flame Retardants," for CPSC, NASEM is already familiar with the project and can build on the case developed in the committee's case-studies portion of the previous study.

Pro: The NASEM pilot project would provide expert advice through conducting a portion of the required work for OFR risk assessment, which also would serve as a detailed template for further work performed by NASEM or by CPSC staff or contractors.

Con: The work would include only the hazard assessment step of the multistep process, for one subclass.

Con: The NASEM process does not allow for frequent interactions between staff and the committee; NASEM committees work independently from sponsors.

Con: NASEM committees may not be able to make adjustments or be amenable to mid-stream changes, based on findings in parallel activities or other factors.

Con: Cross-disciplinary coordination for hazard and exposure assessment is more difficult because different organizations are completing the work, and the independent NASEM committee process could prevent timely interactions with other organizations.

Con: Can be relatively time- and resource-consuming.

7. Staff Conclusions

Staff recommends that the Commission direct staff to proceed with assessing the potential health risks of OFRs in specified consumer products using a class approach. In this memo, staff outlines the general process for performing class-based risk assessments, and provides recommendations for specific approaches and tasks.

Key recommendations include:

1. For FY 2021, perform work through contractors, directed and monitored by staff. Staff estimates that the proposed contracts together would cost about $1.5 million (the above baseline appropriations in the Performance Budget Request). Although there are advantages to having the NASEM conduct a pilot study, staff concludes that using NASEM is not the most time- and cost-effective approach.
2. Begin by completing scope documents and analysis plans for several classes, then prioritize classes to begin hazard and exposure assessment tasks.
3. Publish scope documents and analysis plans for public comment.
4. Complete hazard identification and exposure assessment work in parallel.
5. Peer-review each draft class-specific risk assessment.
6. Make staff recommendations on whether to proceed with class-based risk assessment after each class-specific scope document is completed.
7. Make staff recommendations on whether to proceed with rulemaking after each class-specific risk assessment is completed.
8. Use a CHAP, if required, before initiating rulemaking if the risks include carcinogens, mutagens, or reproductive/developmental hazards.

TAB A: Technical Approach to Hazard Assessment Using Class-Based Approach

TAB A

TECHNICAL APPROACH TO HAZARD ASSESSMENT USING CLASS-BASED APPROACH

Hazard identification and dose-response assessment are the first two steps of risk assessment. The following provides additional details on the approach that the CPSC staff will use to assess the potential health hazards of OFRs. The staff's approach will combine the recommendations of the National Academies of Science, Engineering, and Medicine (NASEM) report on OFRs[1] with the risk assessment methods used by CPSC[2] and other agencies. Hazard assessment identifies potential adverse health effects caused by chemicals or products and assesses the evidence that an effect may occur in humans. CPSC classifies hazards as "possibly," "probably," or "known" to be toxic in humans, relying primarily on human and animal data. Dose response is a quantitative estimate of toxic potency.

Assessing hazards of chemicals, whether individually or in classes, depends on the availability of relevant toxicity data. In a class-based approach, in particular, there must be adequate data on one or more class members or close analogs to assess toxicity. To fill data gaps for data-poor class members, a class-based hazard assessment may need to rely on application of computational methods and new approach methodologies (NAMs), in addition to available data from research animals and epidemiological studies. Whereas a single chemical risk assessment generally considers the most sensitive adverse health endpoint for that chemical, the class approach considers endpoints that are common among class members.

Hazard Identification Process for the Class-Based Approach

CPSC staff plans to scope the class-based hazard assessments through initial literature surveys and development of analysis plans.

Literature Survey

CPSC staff and their contractors will conduct a literature survey for each of the 14 subclasses to understand data availability and identify possible health endpoints. Staff may choose to move forward with additional work on one or more subclasses before completing literature surveys for all 14 subclasses. The literature surveys will begin with secondary sources, such as assessments completed by authoritative bodies, such as the National Toxicology Program (NTP), Environmental Protection Agency (EPA), and the International Agency for Research on Cancer (IARC). Staff will also search the peer-reviewed literature using toxicity databases enriched for hazard information (Table A1). Toxicity databases and tools are also discussed in Tab C.

CPSC staff will search by chemical names, synonyms, and CAS Registry Number® (CAS RN®). The literature survey will focus on readily available information from completed assessments, completed literature reviews, and toxicity databases. The toxicity of OFRs may

[1] National Academies of Sciences, Engineering, and Medicine (NASEM) 2019. A Class Approach to Hazard Assessment of Organohalogen Flame Retardants. Washington, DC: The National Academies Press. https://doi.org/10.17226/25412. Available at: http://nap.edu/25412.

[2] CPSC (1992) Labeling requirements for art materials presenting chronic hazards; guidelines for determining chronic toxicity of products subject to the FHSA; supplementary definition of "toxic" under the Federal Hazardous Substances Act; final rules. Federal Register 57: 46626-46674. https://www.cpsc.gov/s3fs-public/pdfs/blk_pdf_chronichazardguidelines.pdf

include both acute and chronic health effects, although the focus of the assessments will most likely be chronic effects. Chronic health effects include any persistent health effect, such as carcinogenicity, neurotoxicity, reproductive and developmental effects, or chronic organ toxicity effects, such as hepatotoxicity, renal toxicity, respiratory toxicity, or endocrine system effects.

Table A1. Examples of Hazard Data Sources for Literature Surveys

Reference	Description	URL
International Agency for Research on Cancer (IARC)	Authoritative reviews on potential carcinogens	https://monographs.iarc.fr/agents-classified-by-the-iarc/
Report on Carcinogens (RoC)	Authoritative reviews on potential carcinogens	https://ntp.niehs.nih.gov/whatwestudy/assessments/cancer/criteria/index.html
Chemical Effects on Biological Systems	NTP database with data from academics, industrial, and government labs.	https://manticore.niehs.nih.gov/cebssearch
Integrated Risk Information System (IRIS)	Database of EPA toxicological reference values	https://www.epa.gov/iris
California Proposition 65	Reviews of potential carcinogens and reproductive/developmental toxicants	https://oehha.ca.gov/proposition-65/proposition-65-list/
Agency for Toxic Substances and Disease Registry (ATSDR)	Authoritative reviews on chemicals	https://www.atsdr.cdc.gov/
Health Canada Chemicals Management Plan	Database of hazard and risk assessment	https://www.canada.ca/en/health-canada/services/chemical-substances/fact-sheets/chemicals-glance.html#a2
PubMed	Database of references and abstracts on life sciences	https://pubmed.ncbi.nlm.nih.gov/
ToxRefDB	Database of toxicological reference values	https://catalog.data.gov/dataset/toxicity-reference-database-bcf19
Tox21	Database of high throughput test data	https://ntp.niehs.nih.gov/whatwestudy/tox21/index.html
ToxCast	Database of high throughput test data	https://www.epa.gov/chemical-research/exploring-toxcast-data-downloadable-data
EPA CompTox Chemicals Dashboard	Database of toxicology and chemistry information	https://comptox.epa.gov/dashboard
Organisation of Economic Co-operation and Development (OECD) QSAR toolbox	Database of toxicology and chemistry information	https://www.oecd.org/chemicalsafety/risk-assessment/oecd-qsar-toolbox.htm
National Toxicology Program (ICE)	Integrated Chemical Environment (ICE) curated databases of toxicology information	https://ice.ntp.niehs.nih.gov/

Analysis Plan

The results of the literature survey must be screened to identify the types of data available from each reference. The screening process, which is labor intensive, may be facilitated by use of readily available specialized software to identify articles of interest. Based on the results of the literature survey and screening, staff will generate an evidence table or map for each class, which will summarize the toxicity data available for chemicals in each class. This summary will identify common health endpoints, types of studies for data-rich and data-poor chemicals (Table A2), and data gaps for a class. This information will be used to develop an analysis plan. The analysis plan describes the objectives of the hazard assessment, including the health endpoints of interest and relevant data specific to the subclass, and establishes the process for proceeding with the hazard assessment. The analysis plan includes the development of inclusion and exclusion criteria in a PECO statement.[3] PECO refers to population (P), exposure (E), comparator (C), and outcomes (O) of interest. The PECO statement essentially describes the scope of the literature search and subsequent analysis.

Table A2. Toxicity Data Types

Hazard Evidence Type	**Short Definitions/Examples**
Human	Epidemiological studies that observe associations between reported or measured exposures and diagnosed health effects.[4]
Animal	Studies in laboratory animals that use defined exposures or doses, through oral, inhalation, and dermal routes and observations of responses, including acute effects, carcinogenicity, effects on reproduction and development, endocrine disruption, target organ effects, neurotoxicity, immunotoxicity, sensitization, irritation.
Toxicokinetics	Studies (in animals or humans) that determine the bioavailability and ADME (absorption, distribution, metabolism, and elimination) patterns for a chemical over time.[5]
Other studies (NAMs, in silico/computational, mechanistic)	Studies using animal or human cells and tissues, *i.e.*, in vitro assays, ex vivo studies.
	Alternative animal species, such as zebrafish and nematodes.
	Modeled estimates based on QSAR, read-across, and other methods.

Literature Search, Data Extraction

Based on the completed literature surveys and analysis plan development, staff will proceed with a literature search for the class of interest. The goal of the literature search is to identify all

[3] Rooney AA, Boyles AL, Wolfe MS, Bucher JR, Thayer KA. Rooney AA, et al. Systematic review and evidence integration for literature-based environmental health science assessments. Environ Health Perspect. 2014 Jul;122(7):711-8. doi:10.1289/ehp.1307972.

[4] Epidemiological studies also provide exposure information and are an exposure data type.

[5] Toxicokinetic studies may overlap with human biomonitoring studies, which are an exposure data type.

relevant studies that can potentially be used to assess the toxicity end points specified by the analysis plans for the subclass, within the bounds of the PECO statement. Staff will consider relevant data sources, as in the literature survey step, as well as bibliographic databases (*i.e.*, PubMed, Web of Science, and Google Scholar), with a focus on data types described in the analysis plan, *i.e.*, human data, animal data, in vitro data, NAM data, and in silico data. The literature search will be conducted through a comprehensive and consistent approach, using methods similar to those used in systematic review. The search will focus on selected endpoints, study types, and populations identified in the analysis plan. Search terms will include chemical names, synonyms, and CAS RN.® Other search terms could focus on toxicity data types or endpoints, *e.g.*, cancer, carcinogenicity, or other health effects identified in the literature survey. Search terms may also include toxicology terms, such absorption, distribution, metabolism, and excretion (ADME) studies. In addition to these traditional toxicity terms, staff will search for data and information related to NAMs and computational approaches, with terms such as zebrafish, in vitro, adverse outcome pathway (AOP), mode of action (MOA), QSAR, and read-across.

Once relevant studies have been identified, study methods and data will be extracted and summarized for further analysis. Information to be extracted will include chemical name and other identifiers, study design, details of the animal model or population studied, doses, toxicity endpoints, study results, statistical methods, and other study details. Data extraction is a labor-intensive process that generally requires at least two individuals to review each reference. Data extraction may be facilitated by using specialized software tools developed for systematic review, such as LitStream™ or DistillerSR.

Data Evaluation and Integration

Once the relevant data have been extracted, the data will be evaluated for quality, usefulness, and relevance. CPSC's Chronic Hazard Guidelines[6] address factors to consider in evaluating epidemiological and toxicological data. Data evaluation will consider data quality, data sufficiency, data consistency, and data relevance. Factors that need to be considered in data quality evaluation may include the number of animals tested, data variability, dose ranging, and the use of appropriate statistical methods. Data sufficiency refers to whether there are enough data to address the questions established in the project scope and analysis plan. Data consistency refers to the degree of agreement in the available data for particular endpoints. Data relevance refers to the extent to which data and tests are appropriate for human health assessment and specified toxicity endpoints, such as selection of animal model, including life stage, and dose considerations, including routes of dosing or exposure.

Once the data have been evaluated, the next step is to integrate the data to determine potential hazards of chemicals or chemicals classes. The class-based approach relies on the availability of data across members of a subclass, and is based on common biological activity or toxicity endpoints among subclass members; but the integration concept is otherwise similar for individual chemicals and groups of chemicals. Staff plans to approach the synthesis and

[6] CPSC (1992) Labeling requirements for art materials presenting chronic hazards; guidelines for determining chronic toxicity of products subject to the FHSA; supplementary definition of "toxic" under the Federal Hazardous Substances Act; final rules. Federal Register 57: 46626-46674. Available at: https://www.cpsc.gov/s3fs-public/pdfs/blk_pdf_chronichazardguidelines.pdf.

integration of data for class members through a combination of the CPSC Chronic Hazard Guidelines and the recommendations of the NASEM committee for a class approach. The goal in a class approach is to reach a determination about toxicity of the class.

One possible approach to class-based hazard identification is to use data-rich class members to understand toxicity and mechanisms of effects across the class. Data-rich chemicals could be used to interpolate or extrapolate to data-poor class members, given sufficient data of various types to support such analyses. The NASEM committee suggested several approaches and tools for analysis of OFR classes, including read-across, structure-activity relationships, or quantitative structure-activity relationships (QSAR), in vitro to in vivo extrapolation (IVIVE), as well as limited testing, such as with new approach methodologies (NAMs). In the case that available information indicates that chemicals within a subclass are too heterogeneous or inconsistent (discordant), or data are not sufficient to support a determination about hazard, additional analysis might be necessary to support conclusions that are applicable to the subclass. This might include obtaining additional data or reclassifying the members of the class.

Using New Approach Methodologies for Classes

The term new approach methodologies (NAM or NAMs) refers broadly to 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.[7] NAM studies may include approaches, such as 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. Staff notes that using such methods and approaches is not yet widespread in regulatory settings, although certain applications of NAM approaches to inform decision-making may be advancing (*e.g.*, in priority setting or providing support for decisions based on more traditional data. Although CPSC staff plans to consider NAM data for use in hazard assessment, this determination will need to be made on a class-by-class basis, considering the overall body of data for a subclass, and the specific applications of NAM for chemicals in a subclass. This section briefly summarizes tools and approaches that could be used in class-based assessment.

Read-Across

Read-across is any methodology in which endpoint information for one chemical (source) is used to predict the same endpoint for another chemical (target) that is considered to be similar in some way (*e.g.*, structural similarity or the same mode or mechanism of action). Numerous recent publications describe some of the tools and applications of read-across approaches, including a recent paper addressing potential applications in U.S. federal agencies.[8] Given the application of read-across approaches under European chemicals requirements, the Organisation

[7] EPA, 2018, Strategic Plan to Promote the Development and Implementation of Alternative Test Methods Within the TSCA Program, Available at https://www.epa.gov/sites/production/files/2018-06/documents/epa_alt_strat_plan_6-20-18_clean_final.pdf.

[8] Patlewicz et al., Exploring current read-across applications and needs among selected U.S. Federal Agencies. Regul Toxicol Pharmacol. 2019 Aug;106:197-209. doi: 10.1016/j.yrtph.2019.05.011.

of Economic Co-operation and Development (OECD)[9] and the European Chemicals Agency (ECHA)[10] have also published detailed technical guidance. In the United States, interest in understanding the hazards of another potentially large group of chemicals—per- and polyfluorinated substances, or PFAS—has prompted agencies to incorporate read-across methods into assessments. For example, a Massachusetts state agency recently used read-across in a reassessment of a group of longer chain PFAS to support drinking water regulations,[11] and EPA and NTP staff recently published an approach for studying PFAS that included consideration of read-across applications.[12] The experience to be gained by reviewing federal and state agency scientists' ongoing assessments of PFAS could inform CPSC staff's approach to addressing groups of OFRs, given the similar scope and data availability challenges of assessing large groups of OFRs and PFAS.

NAM Data to Support Read-Across

NAMs may play a key role in a class approach by providing evidence that class members or close analogs share hazard-associated characteristics, even in the case in which traditional animal toxicity data or epidemiological data are not uniformly available for all class members. For example, NAMs may provide mechanistic or other information to demonstrate that the members of a class have similar biological activity. Thus, NAMs can provide a linkage between the data-rich and data-poor members of a class.

QSAR

Structure-activity relationships relate structural features or physicochemical properties of chemicals to chemical or biological activity. They may be qualitative (SAR) or quantitative (QSAR). QSAR has been employed for many years in chemistry, [13,14] toxicology,[15] and more recently, in drug development. In particular, computer-assisted SAR has been used to predict adverse health effects by searching for "structural alerts," *i.e.*, functional groups associated with cancer or other health effects. SAR can be used by risk assessors in a variety of contexts interested in evaluating any of the large number of existing and new chemicals that lack

[9] OECD.2014. Guidance on Grouping of Chemicals, Second Edition, ENV/JM/MONO(2014)4. Available at: https://www.oecd.org/publications/guidance-on-grouping-of-chemicals-second-edition-9789264274679-en.htm.
[10] ECHA. 2017. Read-Across Assessment Framework (RAAF). European Chemicals Agency. Available at: http://echa.europa.eu/documents/10162/13628/raaf_en.pdf.
[11] Massachusetts Department of Environmental Protection, 2019 Per- and Polyfluoroalkyl Substances (PFAS): An Updated Subgroup Approach to Groundwater and Drinking Water Values. Available at: https://www.mass.gov/files/documents/2019/12/27/PFAS%20TSD%202019-12-26%20FINAL.pdf.
[12] Patlewicz et al., A Chemical Category-Based Prioritization Approach for Selecting 75 Per- and Polyfluoroalkyl Substances (PFAS) for Tiered Toxicity and Toxicokinetic Testing. Environ Health Perspect. 2019 Jan;127(1):14501. doi:10.1289/EHP4555.
[13] Hammett, L. P. J. The Effect of Structure upon the Reactions of Organic Compounds. Benzene Derivatives. J. Am. Chem. Soc. 1937, 59, 96.
[14] Woodward, R. B. (1941). Structure and the Absorption Spectra of α,β-Unsaturated Ketones. J. Am. Chem. Soc. 63 (4): 1123. doi:10.1021/ja01849a066.
[15] Swain C.G., Scott, C.B. 1963. Quantitative Correlation of Relative Rates. Comparison of Hydroxide Ion with Other Nucleophilic Reagents toward Alkyl Halides, Esters, Epoxides and Acyl Halides. J. Am. Chem. Soc. 75: 141-147.

complete or relevant toxicity data, and by others seeking to add to understanding chemical properties and biological activity.

Numerous publications[16] and guidance documents[17,18] have been developed that address developing and applying QSAR models. Over time, QSAR models have been incorporated into software packages (freely available from public resources or in commercially-available programs).[19] The robustness of the QSAR approach is largely dependent on the quality and relevance of data used to develop models and the appropriate use of available QSAR software. QSAR models can be used to predict a range of chemical characteristics, such as physicochemical properties, possible metabolism, receptor binding, and other mechanistic information, and toxicity endpoints, such as genotoxicity, skin sensitization, and various types of chronic toxicity. The utility of QSAR approaches for a given chemical or group of chemicals depends on availability of data on appropriate analogue chemicals and the applicability of validated models for the chemicals and endpoints of interest. Depending on information needs, CPSC staff plans to integrate QSAR results with other data to support hazard conclusions for OFR classes.

Tox21 and ToxCast

The Tox21and ToxCast programs consist of a number of high-throughput, in vitro assays that focus on known toxicity pathways. The NASEM committee searched Tox21 and ToxCast data on OFRs. NASEM identified 43 assay endpoints for 39 OFRs in the Tox21 database, and 171 assay endpoints for 39 OFRs from ToxCast. CPSC staff could update the data search for Tox21 and ToxCast, as needed, by using the NASEM approach, and supplement with data from the literature in bibliographic databases. Since most of the Tox21 and ToxCast are designed to identify outcome pathways for a given toxicological endpoint, they provide valuable mechanistic information. Limitations for high-throughput Tox21 and ToxCast include insufficient metabolic capability and a limited number of assays available for certain endpoints, such as thyroid toxicity. In addition, most of the in vitro systems are designed for a single molecular event, such as a key initiating event in a pathway, rather than apical endpoints, such as cancer or organ toxicity.

Zebrafish Assays and Alternative Animal Models

The zebrafish assay is an alternative animal model, in the category of NAMs, which has been studied for use in toxicity evaluations, especially for developmental toxicity, embryotoxicity, and neurotoxicity. One advantage of the zebrafish model is the relatively large amount of scientific information about this animal, such as embryology, which provides a scientific foundation for

[16] See, for example, Walker JD et al., Guidelines for developing and using quantitative structure-activity relationships. Environ Toxicol Chem. 2003 Aug; 22(8):1653-65. DOI: 10.1897/01-627.
[17] OECD, Guidance Document on the Validation of (Quantitative) Structure-Activity Relationships [(Q)SAR] Models, ENV/JM/MONO(2007)2. Available at: https://www.oecd.org/env/guidance-document-on-the-validation-of-quantitative-structure-activity-relationship-q-sar-models-9789264085442-en.htm.
[18] North American Free Trade Agreement (NAFTA) Technical Working Group on Pesticides (TWG), (Quantitative) Structure Activity Relationship [(Q)SAR] Guidance Document, November, 2012. Available at: https://www.epa.gov/sites/production/files/2016-01/documents/qsar-guidance.pdf.
[19] See, for example, Gatnik and Worth, Review of Software Tools for Toxicity Prediction, JRC Technical Report EUR 24489 EN – 2010. Available at: https://publications.jrc.ec.europa.eu/repository/handle/JRC59685.

toxicity studies. Another advantage of the zebrafish model is the high fertility and relatively fast embryonal development of zebrafish; zebrafish embryos are fertilized externally and are transparent through the early days of life, thus allowing for non-invasive observation of exposure-related effects. In two case studies, the NASEM OFR committee used zebrafish data to illustrate possible approaches to class-based hazard analysis. CPSC staff plans to consider any available zebrafish data, for example, for trialkyl phosphates OFRs. In addition, CPSC staff could use zebrafish data to fill gaps in the more traditional sources of data, such as by providing mechanistic support for hazard conclusions about chemicals and chemical classes. Staff notes that, as with any other model, zebrafish assays have limitations, and staff will need to evaluate this model, and each individual study, for quality and relevance.

Obtaining New Hazard Data

For some data-poor classes or chemicals, it may be necessary to obtain new toxicity data. The need for new data may become apparent at any stage of the hazard assessment from the literature survey stage through the draft risk assessment. For example, additional data may be needed to resolve discordant data for a chemical or chemical class. CPSC staff has limited options for obtaining new hazard data. The primary option is to nominate chemicals for testing by the National Toxicology Program (NTP). Other options include: (*i*) Nominate chemicals for testing through EPA's Interagency Testing Committee (ITC); EPA can request submission of existing, unpublished data or issue a testing rule to require companies to perform certain tests. (*ii*) Work with contract research organizations to perform tests; this option requires CPSC to pay testing costs. (*iii*) Establish interagency agreements with other federal agencies to perform testing; in this case, the other federal agency might share the cost, if the needs of both agencies are similar. Regardless of who conducts or funds the tests, traditional animal tests are expensive and take years, or even decades, to complete. For example, of the studies that the CPSC staff nominated to NTP in 2005, the study on antimony trioxide was completed in 2017, and the study on tris(chloropropyl) phosphate was completed in 2020. The study on aromatic phosphates is still underway.

Therefore, any attempts to obtain new hazard data will proceed with a tiered approach that initially relies on new alternative methods, in vitro assays, and toxicity testing with alternative animal species. The results of those studies can help to identify potential end points of interest in the subclass. In some cases, for example, data-poor classes, targeted animal toxicity studies could be needed. The strategy in such a plan will be to address gaps in knowledge about OFR classes in a cost- and time-efficient manner.

Approaches for Dose-Response Analysis for Classes

Dose-response assessment is a quantitative estimate of the toxic potency of a chemical. Dose-response assessment typically relies on data from studies in experimental animals, and may involve extrapolation from the relatively high doses of laboratory studies to the lower-dose levels that more closely match potential human exposure levels. CPSC staff typically uses dose-response models to estimate the acceptable daily intake (ADI) for non-carcinogens or the cancer

unit risk (potency factor) for carcinogens.[20] These methods require adequate data, such as studies with multiple dose levels. Thus, data-rich class members are generally more amenable to dose-response assessment.

The NASEM committee suggested several options for data-poor chemicals in class-based dose-response assessments.[21] One option is to use the most potent chemical in the group as a surrogate for the group. This approach tends to be conservative, that is, more protective of public health, unless a data-poor member is more toxic than the surrogate. This approach is useful for a preliminary risk assessment. If the risk from the most toxic member of the class is low enough to conclude that there is a negligible risk to consumers, then there is no need to proceed any further. However, if the analysis indicates a significant risk, it may be necessary to obtain more toxicity information on the data-poor members of the class to replace the conservative assumption (*i.e.*, that all members of the class are as potent as the most toxic member) before proceeding to a final risk assessment or a regulatory process. Some class members could be less toxic and pose a negligible risk,[22] in which case, the conservative choice to use the most potent chemical as a surrogate for the class would not be supported. An alternative to using the most toxic member of the class as a surrogate is to assume that the potencies of the data-poor members lie within the range of potencies of the data-rich members of the class.[23]

Another approach is to use relative potency factors (RPFs) or toxic equivalence factors (TEFs), which have been used for class-based and mixtures assessments for various chemicals, including dioxins,[24] polycyclic aromatic hydrocarbons (PAHs)[25] and phthalates.[26,27] RPFs and TEFs present the toxicity of class members relative to one class member, the index chemical. At least one class member (the index chemical) must have sufficient data for conventional dose-response assessment. Data from short-term animal studies can be used to estimate the toxicity of the other class members, relative to the index chemical.

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[20] CPSC (1992) Labeling requirements for art materials presenting chronic hazards; guidelines for determining chronic toxicity of products subject to the FHSA; supplementary definition of "toxic" under the Federal Hazardous Substances Act; final rules. Federal Register 57: 46626-46674. https://www.cpsc.gov/s3fs-public/pdfs/blk_pdf_chronichazardguidelines.pdf.

[21] Ibid., NASEM, pp. 17-18.

[22] Babich MA (2006) CPSC Staff Preliminary Risk assessment of Flame Retardant (FR) Chemicals in Upholstered Furniture Foam. U.S. Consumer Product Safety Commission, Bethesda, MD. December 21, 2006.

[23] Ibid., Babich MA (2006).

[24] EPA (2010) Recommended Toxicity Equivalence Factors (TEFs) for Human Health Risk Assessments of 2,3,7,8-Tetrachlorodibenzo-p-dioxin and Dioxin-Like Compounds. Risk Assessment Forum, Environmental Protection Agency, Washington, DC. December 2010. EPA/100/R-10/005. https://www.epa.gov/sites/production/files/2013-09/documents/hhtef_draft_090109.pdf.

[25] CPSC (1995) Report on the Cancer Risk from Exposure to Polycyclic Aromatic hydrocarbons (PAH's) in Indoor Air Emissions from EPA-Certified (Phase II) Wood Stoves. U.S. Consumer Product Safety Commission, Bethesda, MD. June 30, 1995.

[26] CHAP (2014) Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives. U.S. Consumer Product Safety Commission, Bethesda, MD. July 2014. http://www.cpsc.gov/chap.

[27] Lioy, P.J., Hauser, R., Gennings, C., et al., 2015. Assessment of phthalates/phthalate alternatives in children's toys and childcare articles: review of the report including conclusions and recommendation of the Chronic Hazard Advisory Panel of the Consumer Product Safety Commission. J. Expo. Sci. Environ. Epidemiol. 25, 343–353.

Another approach to dose-response analysis is to use in vitro to in vivo extrapolation (IVIVE) to convert quantitative measurements of in vitro biological activity to human relevant doses. Comparison of these estimated doses to doses used or derived through other methods may help to refine class-based dose-response analysis.[28] The read-across methods used for hazard identification (see above) may be adapted to dose-response assessment, provided that they provide quantitative dose response or potency data. For example, NAM or QSAR data might be used as a framework for interpolation or extrapolation from data-rich to data-poor chemicals. To have confidence in this approach, the NAM or QSAR data must accurately predict the toxicity of the data-rich chemicals before being used to predict the toxicity of the data-poor chemicals. Since data availability for data-poor chemicals is limited, the data consistency level between data-rich chemical and data-poor chemical determine whether data-rich chemical conclusions can apply to the whole class, or to the data-poor chemicals.

[28] Paul Friedman, K., Gagne, M., Loo, L. H., et al. (2020). Utility of In Vitro Bioactivity as a Lower Bound Estimate of In Vivo Adverse Effect Levels and in Risk-Based Prioritization. Toxicological Sciences, 173(1), 202-225.

TAB B: Technical Approach to Assess Exposures Using a Class-Based Approach

TECHNICAL APPROACH TO ASSESS EXPOSURES USING A CLASS-BASED APPROACH

SCOPING THE EXPOSURE ASSESSMENT

CPSC staff plans to begin class-based exposure assessments by identifying potential sources of exposure and depicting these through a conceptual model. CPSC staff plans to research available market-use information to identify end-use applications of OFR chemicals. Tab D provides more detail on Market-Use Profiles. CPSC staff also plans to research additional contextual information obtained from Market-Use Profiles when characterizing OFR chemicals used in consumer products:

- Material type: chemical substances added to solid matrices have variable potential to emit or migrate from these solid matrices, depending on the properties of the material. The temperature, density, structure, thickness, and exposed surface area are all likely to vary for different material types.[1]
- Physicochemical properties: Chemical substances within each OFR class have variability in physicochemical properties that inform their potential to emit or migrate and their subsequent fate and transport in indoor environments. Measured and estimated physicochemical properties will be arrayed as part of source characterization.[2]
- Where and how product is used: The physical location of a product (*i.e.*, within the living space, in an attic, behind a wall, outdoors) informs exposure potential. The typical life-span of a product in an indoor environment, how people interact with the product through routine contact, and characterization of the indoor environment where the product is used also inform exposure potential.[3]

Literature Survey: Identify readily available information

CPSC staff plans to use information from completed exposure and risk assessments and database sources. Reviewing these data sources will inform development of likely exposure scenarios. These qualitative exposure scenarios will inform CPSC staff's literature search analysis plan. Tab C provides more detail on readily available exposure databases. CPSC staff plans to integrate information on OFR sources and potential exposures into a conceptual model. Conceptual models visually represent potential exposure sources, pathways, receptors, and effects.

[1] EPA 2017. Indoor Exposure Testing Protocols Version 2.0. Available at: https://www.epa.gov/sites/production/files/2018-01/documents/indoor_exposure_testing_protocols_version_2.pdf
[2] EPA 2019. Consumer Exposure Model 2.1 User Guide. Available at: https://www.epa.gov/sites/production/files/2019-06/documents/cem_2.1_user_guide.pdf
[3] OECD 2018. Harmonized Template for Use and Exposure Information: 305 Consumer Uses. Available at: https://www.oecd.org/ehs/templates/harmonised-templates-use-exposure-information.htm

Analysis Plan

The results of the market-use profile and the literature survey can be used to identify the types of readily available exposure data for chemicals within the subclass. Based on the results of the literature survey and screening, staff will understand where readily available data are and are not available, and use this information to plan a class-based literature search. Table B1 provides descriptions of exposure data types.

CPSC staff proposes grouping exposure data into data types. Due to the heterogeneous nature of exposure data, accurate classification of exposure data is paramount. This classification ensures that applicable and useful information is applied to relevant chemical and product groups within classes. It is possible for a study to contain multiple exposure data types. In fact, these studies tend to be the most useful because they provide important context that connects exposure sources, pathways, and receptors.

Table B1: Exposure Data Types and Definitions

Exposure Data Type	Short Definition
Environmental monitoring	Measured concentration(s) obtained from sampling and analysis of chemical(s) in environmental media. Monitoring data include indoor media (*i.e.*, indoor air, indoor dust, and indoor surfaces) and media that may be influenced by consumer products (*i.e.*, indoor media, food, soil, water, air).
Biomonitoring	Measured concentration(s) obtained from sampling and analysis of chemical(s) in biological matrices. Biomonitoring data include biomarkers of internal exposure (*i.e.*, blood, urine, breastmilk, lipids, and organs) and personal, external measurements of exposure (*i.e.*, dermal wipe sampling, personal breathing zone samples).[4]
Modeled environmental concentrations	Calculated chemical concentration(s) present in an environmental media based on parameter inputs (*i.e.*, product source inputs, physicochemical properties, building values) associated with the exposure scenario of interest.
Modeled internal doses	Calculated chemical dose(s) present in a human receptor following uptake (*i.e.*, age-specific average daily dose, lifetime average daily dose).
Experimental, product testing	Data obtained from experimental studies with controlled and pre-determined testing conditions. Product testing data to determine chemical content present in products, emission of chemicals from products to air or dust, partitioning of chemicals between products air dust or sinks, and migration of chemicals from products to biological matrices, such as saliva or skin.
Chemical/Product Source characterization	Data obtained through reporting, surveys, or databases that contain information on how chemicals are used in products, contain information on how consumers use or interact with products (activity patterns), or contain inherent physicochemical properties of chemicals or materials.
Epidemiological data	Data obtained from observational studies that examine relationships between exposed groups or individuals and observed health outcomes.[5] Quantitative exposure data described in epidemiological study should be related to exposure scenario of interest.

[4] Human biomonitoring studies may overlap with toxicokinetics studies.
[5] Epidemiological studies also provide toxicity (health effects) information and are a toxicity data type.

LITERATURE SEARCH: IDENTIFYING AND EVALUATING RELEVANT DATA FOR THE EXPOSURE ASSESSMENT

Identify additional available information

CPSC staff plans to compile any relevant information from literature searches for use in exposure assessment. Staff will search for literature in bibliographic databases (*i.e*., PubMed, Web of Science, and Google Scholar), using chemical names, identifiers, and synonyms for chemicals within the class. CPSC staff will use keywords to screen retrieved results. For example, the following keywords could be used for data screening and are grouped by exposure data type:

- Environmental monitoring: monitor, sample, analyze, detect, occur, "indoor dust," "indoor air," diet, food;
- Biomonitoring: monitor, sample, analyze, detect, occur, "breast milk," blood, lipid, urine, NHANES, sera, hair, tissue;
- Experimental Product Testing: "emission rate," "emission factor," "chamber concentration," "migration rate," "indoor air," "indoor dust," saliva, sweat, sebum, skin, contact, loading;
- Chemical/Product Source characterization: "consumer product," "product test," "chemical concentration," formulation, "product use," "building material," "class-specific material types informed by scope documents" ;
- Modeled Environmental Concentrations: input, fate, transport, transfer, emission, source, indoor environment, volume, air exchange, "indoor air," "indoor dust," SVOC;
- Modeled Doses: average daily dose, lifetime average daily dose, average daily exposure, "exposure factor," age, receptor;
- Epidemiological data: observation, population, exposure, effect, longitudinal, cross-sectional, case-control, prospective, retrospective, association, bias, questionnaire. Epidemiology studies are a source of both exposure and hazard information.

CPSC staff plans to screen data for relevancy, identify data types, and match the data to chemical classes and chemical substances. CPSC staff acknowledges that certain classes have well-studied chemical substances within the class. Staff will use existing completed assessments and recent literature reviews to help identify relevant data sources.

Evaluate and Integrate information

CPSC staff plans to evaluate exposure data to determine overall relevance and reliability for use in OFR exposure assessment.[6] CPSC staff acknowledges that different types of exposure data will likely require different approaches for data evaluation.[7] CPSC staff plans to tier data

[6] Udesky, J. O., Dodson, R. E., Perovich, L. J., & Rudel, R. A. (2019). Wrangling environmental exposure data: guidance for getting the best information from your laboratory measurements. *Environmental Health*, *18*(1), 99.
[7] EPA 2018. Application of Systematic Review in TSCA Risk Evaluation (2018). Available at: https://www.epa.gov/assessing-and-managing-chemicals-under-tsca/application-systematic-review-tsca-risk-evaluations

evaluation. All studies will receive an initial evaluation for relevance/representativeness and completeness/clarity. In this screen, CPSC staff will determine if the exposure data are relevant for CPSC's use in estimating human exposures from consumer uses and other sources of OFRs. For example, measurements of OFRs in deep lake sediment cores, the upper atmosphere, or remote environments (arctic/Antarctic) are not directly relevant to CPSC's scope, while measurements of OFRs emitted from consumer products into indoor environment are directly relevant to CPSC's scope. The first tier data evaluation will also consider whether all components of the data source are available in its full text and related supplementary material. For example, studies are unlikely to be useful if they do not have a full-text readily available, have very limited or no discussion of methods, or provide incomplete or unclear results. CPSC staff anticipates that a first-tier data evaluation review will reduce the number of remaining studies for more robust data evaluation. In subsequent data evaluations, CPSC staff plans to consider other factors, such as the soundness and validity or sampling and analytical approaches, the characterization of sensitivity, variability, and uncertainty, the incorporation of QA/QC and level of independent peer review, and finally the degree of relevance for estimating exposure scenarios of interest to CPSC. Staff will also give preference to data that are most recent and relevant to North American products and populations.

CPSC staff plans to integrate exposure data for use in its exposure assessment. Depending on the specific nature of the OFR exposure assessment, a subset of available exposure concentrations or doses from monitoring or modeled estimates may be compiled. For example, CPSC staff may determine that one, among many, biomarkers is more reliable and relevant for chemicals in a subclass. CPSC staff may determine that de-novo, fit for purpose, modeled estimates of exposure are more reliable and relevant for use in exposure assessment rather than relying on previous modeled estimates of exposure that used heterogeneous and dated input assumptions. While CPSC staff plans to evaluate all exposure information, CPSC staff will provide a transparent rationale for choices made to select certain data for exposure integration.

ITERATING AND COMPLETING THE EXPOSURE ASSESSMENT BY QUANTIFYING EXPOSURE SCENARIOS

CPSC staff plans to follow existing guidance documents and plans to use established approaches when developing class-based exposure assessments, such as the CPSC chronic hazard guidelines. Exposure assessment evaluates the duration, intensity, frequency, and nature of exposures to human populations. Exposure assessment also includes a discussion of exposed populations or subpopulations. Staff plans to evaluate exposure using any or all of the following general approaches:

- Estimates of age-specific doses based on measured environmental monitoring data. This approach uses occurrence data in environmental media (*e.g.*, indoor air, indoor dust, dietary sources, drinking water, ambient air, soil) and combines this data with age-specific exposure factors and activity patterns to estimate dose. CPSC staff will consider the nexus of these empirical observations of presence in the indoor and outdoor environment with likely consumer product use patterns.
- Estimates of age-specific doses based on measured human biomonitoring data. This approach uses occurrence data in biological matrices (*e.g.*, blood, serum, urine, breast milk, fatty tissue) and combines with age and/or sex specific toxicokinetic data to

estimate dose. CPSC staff will also consider the nexus of these empirical observations of presence in biological matrices with likely consumer product sources.

- Estimates of direct consumer exposure through measurements of chemical migration from products to people through direct contact (*i.e*., mouthing, dermal contact)
- Estimates of indirect consumer exposure through measurements of chemical emissions from products to indoor environments (*i.e*., indoor air, indoor dust) and associated time spent in microenvironments.
- Estimates of consumer exposure through use of existing consumer exposure models. These models estimate indoor environmental concentrations and/or doses associated with defined sources (consumer products) used in indoor environments. Models require source inputs (consumer product and chemical substance parameters), environmental inputs (room volume, air exchange, sink area), and population inputs (age-specific exposure factors and activity patterns).
- For chemicals within a class that do not have any measured exposure data, staff may choose to model exposure or to use measured data from a closely related chemical to fill data gaps. Consumer exposure models require inputs of measured or estimated physicochemical properties (*i.e*., water solubility, vapor pressure, octanol-air partition coefficient, octanol-water partition coefficient). Some consumer exposure model inputs are influenced by the material type and the chemical substance (*i.e*., solid-phase diffusion coefficient, gas-phase mass transfer coefficient, material-air partition coefficient). These model inputs can be experimentally measured or estimated through QSAR. For consumer exposure model inputs, CPSC staff plans to consider the relative uncertainty of QSAR modeled estimates compared with measured data for closely related chemicals, when available. Similarly, CPSC staff plans to consider the relative uncertainty of modeled estimates when compared with measured data (*i.e*., exposure concentrations and doses) for closely related chemicals.

Table B2: Guidance Documents for Exposure Assessment

CPSC Chronic Hazard Guidelines	https://www.cpsc.gov/s3fs-public/pdfs/blk_pdf_chronichazardguidelines.pdf
U.S. Environmental Protection Agency (EPA) EXPOBOX	https://www.epa.gov/expobox/about-exposure-factors-handbook
EPA 2019 Guidelines for Human Exposure Assessment	https://www.epa.gov/sites/production/files/2020-01/documents/guidelines_for_human_exposure_assessment_final2019.pdf
EPA 2003 A Summary of General Assessment Factors for Evaluating the Quality of Scientific and Technical Information	https://www.epa.gov/risk/summary-general-assessment-factors-evaluating-quality-scientific-and-technical-information
National Academy of Science Reports	Exposure Science in the 21st Century and related reports
Organisation of Economic Co-operation and Development (OECD) projects under the Working Party on Exposure Assessment	http://www.oecd.org/chemicalsafety/risk-assessment/oecdactivitiesonexposureassessment.htm

CPSC staff plans to consider the following when developing class-specific exposure assessments:

- Variability of physicochemical properties of chemical substances within the class and how this influences properties such as migration from the product into air, suspended particles, settled dust, or liquids or partitioning between phases or media;
- List of equations and explanation of input parameters used for exposure calculations;
- If applicable, discussion of modelling framework and its scientific basis;
- Discussion of the exposure metric used as output for the exposure assessment of chemical(s) within a class. This is informed exposure duration (acute, sub-chronic, chronic, or lifetime) and whether a concentration (mg/m^3) or dose (mg/kg/day) is required to match with toxicity value(s);
- Discussion of variability within the population, based on product or population-specific activity patterns or exposure factors;
- Characterization of exposure information relevant to exposure assessment, including an evaluation of data using weight-of-evidence approaches; and
- Integration of exposure data based on weight-of-the evidence approach. Integration includes discussion on the uncertainties and variability associated with the exposure estimates.

CPSC staff, consistent with CPSC's statutory jurisdiction, plans to focus on consumer applications of OFR chemicals. Consistent with NAS recommendations, CPSC staff will also conceptualize exposures from non-consumer applications of OFRs. Where possible, CPSC staff will estimate aggregate exposure. In this way, the relative source contributions of consumer product exposure can be estimated. Where possible and supported by evidence, CPSC staff will also estimate cumulative exposures for chemicals within the class. In this way, exposures to multiple chemicals over time will be considered.

TAB C: Technical Support Activities for Class-Based Risk Assessment

TECHNICAL SUPPORT ACTIVITIES FOR CLASS-BASED RISK ASSESSMENT

This tab describes the scope of different kinds of work, using examples grounded from past CPSC staff experiences. The primary goal of Tab C is to describe technical support activities that can be used to support class-based risk assessment.

Tab C is organized around the following general areas: prioritization, scoping, and risk assessment.

Prioritization

Staff plans to consider a number of factors to prioritize work on subclasses after completion of initial literature surveys and scope document development. Because of the challenges inherent in managing the complex set of activities required to complete multiple risk assessments, as well as resource limitations at any given point in time, staff will prioritize starting work on subclasses based on availability of hazard and exposure data, an initial assessment of data concordance, and consideration of other readily available information, such as completed assessments for a subclass or for multiple subclass members.

Factors for consideration include:

- Hazard: available data on relevant toxicity endpoints;
- Concordance: available data suggesting concordance across the subclass for one or more toxicity endpoints;
- Exposure: available data suggesting potential exposure, such as documented current or past use in consumer products, widespread occurrence in the indoor environment, human biomonitoring data;
- Regulation: Regulations, restrictions, or risk assessments by other agencies, including international authorities and organizations.

Scope Document

A scope document is developed in the early stages of a risk assessment process. The scope document will include information about a chemical or chemical class, such as chemical names, identifiers, structures, and physicochemical properties, as well as how much relevant data are available, what types of data are available, market-use data, relevant consumer product categories, and staff's plans for proceeding with assessment steps.

Main elements of a scope document include:

- Class identification, physicochemical properties, and regulatory history;
- Literature Survey, PECO statement, and analysis plan;
- Data Evidence Map for Hazard Identification;
- Conceptual Model and Qualitative Exposure Assessment; and
- Market and Use Profile.

Class Identification

The National Academy of Sciences, Engineering, and Medicine (NASEM) organohalogen flame retardant (OFR) committee compiled 14 subclasses using cheminformatics approaches to group chemically and biologically similar chemical substances. Although CPSC staff plans to adopt these 14 subclasses, CPSC staff acknowledges that additional characterization of chemical substances within the subclass may need to occur. Chemical identification is the collection of information that defines a chemical. Each assessment begins with identifying the chemical or chemical class of interest. Staff plans to document the following information: chemical names and synonyms, chemical structures, CAS numbers, and other accepted unique identifiers (*i.e.*, DTXSID[1]), and any reported physicochemical and fate and transport properties. How chemical substances are used and reported can also define subclasses.

Staff plans to consider factors such as feasibility of manufacturing or using a chemical substance on its own or in combination with other closely related chemical substances. For example, there are three primary and several minor stereoisomers of hexabromocyclododecane (HBCD) that have unique chemical identifiers. In practice, these are grouped into a smaller number of more generic HBCD chemical substance identifiers. Similarly, while there are potentially 209 unique polybrominated diphenyl ether (PBDE) congeners, they are typically grouped into a smaller number of more generic PBDE substances. Staff plans to consider whether unique reference standards are available to identify specific OFR chemical substances. Staff also plans to consider how these substances are typically reported when tested. Staff also plans to consider whether there is potential for closely related members of a subclass to be present as minor constituents or impurities in other class members. Staff plans to compile a list of official chemical names, commonly used synonyms, along with class names and identifiers, when executing literature searches. Staff also plans to consider the regulatory history of chemicals within a class, including how other organizations have defined the chemical substance or class.

Literature Survey, PECO Statements, and Analysis Plan

A literature survey is completed before a literature search. Literature surveys provide an initial indication of the relative amount of data available for chemical substances within a class. CPSC staff defines a "literature survey" as a targeted review of information from the following sources:

- Completed assessments by authoritative bodies;
- Database sources; and
- Literature reviews from peer-reviewed literature.

In some instances, organizations, such as NASEM, U.S. Environmental Protection Agency (EPA), Agency for Toxic Substances and Disease Registry (ATSDR), the European Chemicals Agency (ECHA), Australia's National Industrial Chemicals Notification and Assessment Scheme (NICNAS), Japan's National Institute of Technology and Evaluation (NITE), and Health Canada, have already completed toxicity, exposure, or risk assessments, where they have

[1] The DTXSID is a unique substance identifier issued at registration in the chemical registration system underlying EPA's CompTox Chemicals Dashboard

searched, evaluated, and integrated literature. Rather than re-screen and evaluate these studies, CPSC staff plans to directly consider primary studies identified in these completed assessments as a starting point.

CPSC staff has compiled a list of database sources that are expected to provide readily available information on hazard and/or exposure.

Hazard Databases

CPSC staff compiled this overview of databases present in three major tools. These databases include chemical and toxicological data that are derived from a variety of study types and from multiple sources. EPA's CompTox Chemicals Dashboard is freely available and is updated approximately two times a year. The Organisation of Economic Co-operation and Development (OECD) QSAR Toolbox is freely available and is updated over time; the current version is 4.2, released in early 2020. Leadscope® is a subscription-based tool, and is updated over time. CPSC staff notes that available tools can change over time. For example, NASEM relied on eight databases in their literature surveys. One of these databases, TOXNET, is no longer available, and components have been shifted to other platforms. The eight databases largely overlap with the databases shown below.

1. Comparative Toxicogenomics Database
2. EPA Chemistry Dashboard
3. TOXNET (discontinued)
4. ToxCast
5. Tox21
6. Toxicity Reference Database
7. ChemBL
8. PubChem

CPSC staff is developing a search strategy to use database sources and completed assessments to inform a literature survey. Staff may search some or all of these databases. Staff notes that predicted toxicity values, alongside empirical values, are included in these database sources. Staff will ensure that predicted and empirical values are labeled appropriately during the literature survey. Staff notes that consulting multiple databases is needed because there is not one individual database that has compiled all of the available toxicity information.

Table C1: Overview of Hazard Databases

Database	EPA CompTox Chemicals Dashboard[2]	OECD QSAR Toolbox[3]	Leadscope®
ADME database (UK)		X	
Acute Oral toxicity (UNC, EPA)		X	
ATSDR Minimal Risk Levels (MRLs)	X		
Bacterial mutagenicity ISSSTY (Istituto Superiore di Sanità (ISS), Italy)		X	
Biocides and plant protection (ISSBIOC)		X	
Carcinogenicity ISSCAN (ISS, Italy)		X	
Carcinogenic Potency Database (Univ. Calf. Berkley)		X	
Cell Transformation Assay ISSCTA (ISS, Italy)		X	
Chemical Carcinogenesis Research Information System (CCRIS)			X
ChemID plus via EPA TEST	X		
Conditional Toxicity Value Predictor	X		
Dendritic cells (The European Cosmetic and Perfumery Association (COLIPA))		X	
Department of Defense Military Exposure Guidelines	X		
Department of Energy Wildlife Benchmarks	X		
Developmental and Reproductive Toxicity (Proctor and Gamble)		X	
Developmental toxicity (US, International Life Sciences Institute (ILSI))		X	
Developmental toxicity database (Computer Assisted Evaluation of industrial chemical Substances According to Regulations (CAESAR), Italy)		X	
ECHA IUCLID, Registration, Evaluation, Authorisation and Restriction of Chemicals (REACH)	X	X	
EPA Distributed Structure-Searchable Toxicity (DSSTox) Carcinogenicity Potency Database			X

[2] All of the Toxicity Databases in EPA's Chemistry Dashboard are collectively referred to as the ToxVal Database. This database is continually updated and maintained. Existing databases may be expanded, or new databases may be added.

[3] Additional information on OECD QSAR Toolbox data sources is available at: https://qsartoolbox.org/resources/databases/.

Database	EPA CompTox Chemicals Dashboard[2]	OECD QSAR Toolbox[3]	Leadscope®
EPA Integrated Risk Information System (IRIS)	X		
EPA Office of Water Drinking Water Standards	X		
EPA Regional Screening Levels	X		
EPA ToxRef Database	X	X	
European Food Safety Authority (EFSA) Open Food Tox	X	X	
EU COSMOS Project	X		
EU Joint Research Centre (JRC) AcutoxBase	X		
Eye Irritation (European Centre for Ecotoxicology and Toxicology of Chemicals (ECETOC))		X	
FDA Center for Drug Evaluation and Research (CDER) New Drug Application (NDA)			X
FDA Center for Food Safety and Applied Nutrition (CFSAN) Food Contact Notification (FCN)			X
FDA Priority-based Assessment of Food Additives (PAFA) Database			X
GARD Skin sensitization (SenzaGen AB)		X	
Genotoxicity and Carcinogenicity (European Centre for the Validation of Alternative Methods (ECVAM))		X	
Genotoxicity OASIS (Bulgaria)		X	
Genotoxicity pesticides (EFSA)		X	
Hazardous Substances Data Bank Via PubChem	X		
Human Half-life (Arnot Research and Consulting)		X	
Keratinocyte gene expression Givaudan (Switzerland)		X	
Keratinocyte gene expression LuSens (Switzerland)		X	
Micronucleus ISSMIC (Switzerland)		X	
Micronucleus OASIS (Bulgaria)		X	
MUNRO non-cancer (EFSA)		X	
National Toxicology Program (NTP) Chemical Effects in Biological Systems Database			X

Database	EPA CompTox Chemicals Dashboard[2]	OECD QSAR Toolbox[3]	Leadscope®
OECD E-Chem Portal	X		
Oak Ridge National Laboratory (ORNL) Health Effects Assessment Summary Tables (HEAST)	X		
PPRTV	X		
REACH Skin Sensitization (ECHA, Bulgaria)		X	
Receptor Mediated Effects (Bulgaria)		X	
Registry of Toxic Effects on Chemical Substances (RTECS)			X
Rep Dose Tox Fraunhofer ITEM (Germany)		X	
Repeated Dose Toxicity (HESS, Japan)		X	
Rodent Inhalation Toxicity Database (Intl. QSAR Foundation)		X	
Skin Irritation (ECETOC)		X	
Skin sensitization (ECETOC)		X	
Skin sensitization (OECD)		X	
State-Derived Values	X		
ToxCast DB (EPA)	X	X	
Toxicity Japan (MHLW, Japan)		X	
Toxicity to Reproduction (US, National Institute of Environmental Health Sciences (NIEHS))		X	
Transgenic Rodent Database (UK)		X	
Yeast estrogen assay database (Univ. Knoxville)		X	
ZEBET database (Germany)		X	

Exposure Databases

CPSC staff compiled this overview of exposure databases. Staff is developing a search strategy to use database sources and completed assessments to inform a literature survey. Staff may search some or all of these databases. Staff notes that predicted exposure values, alongside empirical values, are included in these database sources. Staff will ensure that predicted and empirical values are labeled appropriately during the literature survey. Staff notes that consulting multiple databases is important because no one database has compiled all of the available exposure information.

Table C2: Overview of Exposure Databases

Database	Description
Biomonitoring California	Collaborative biomonitoring effort (The California Environmental Contaminant Biomonitoring Program), implemented by the California Department of Public Health and the California Environmental Protection Agency
Canadian Health Measures Survey	An ongoing Canadian national survey administered by Statistics Canada in partnership with Health Canada and the Public Health Agency of Canada
Comparative Toxicogenomics Database	A robust, publicly available database of data from published sources that aims to advance understanding about how environmental exposures affect human health.
CDC NHANES	U.S. National Health and Nutrition Examination Survey: National Report on Human Exposure to Environmental Chemicals
EPA Chemistry Dashboard	A compilation of exposure-predictions based on EXPOCAST, information on chemicals reported in products, formulation data for chemicals in products, functional uses of chemicals in products, and links to TRI and TSCA inventory data.
EPA TRI	A compilation of facilities that emit toxic chemicals into the air, water, land of the United States. Includes data on waste transfers.
Inventory/Registration Lists	TSCA Inventory, Health Canada Revised in Commerce List, EU List of Substances Registered under REACH
HBM4EU	European Human Biomonitoring Initiative is a new project compiling existing European biomonitoring data, while adding data for new chemicals over time.
EPA Chemical Data Reporting	Contains production volume, consumer product use, functional use, and formulation data for thousands of chemicals.
U.S. Food and Drug Administration (FDA) Total Diet Study	Ongoing FDA program that monitors levels of about 800 contaminants and nutrients in the average U.S. diet. Database includes data from 2003-2011.
Green Screen Pharos	Common contents/formulation data for many building materials.
Great Lakes Environmental Database	EPA database containing from the EPA's Great Lakes Fish Monitoring and Surveillance Program, an ongoing effort to collect fish from the Great Lakes and analyze them for contaminants.

Information Platform for Chemical Monitoring Data (IPCHEM)	IPCHEM is a web single access point for locating and accessing chemical monitoring data across all media in the European Union.
Minnesota Biomonitoring	MN Biomonitoring Program measures levels of chemicals in Minnesotans.
Consumer Exposure Model Databases	User guides, fact sheets, or databases that have compiled defaults for commonly used consumer exposure models.
Organisation for Economic Co-operation and Development (OECD) Product Release and Exposure Data Warehouse	Database of published release, emission, and exposure data compiled through partnership between US EPA and OECD.
SPIN	SPIN The Substances in Preparations in Nordic Countries databases contains chemical use information from product registries in Norway, Sweden, Denmark, and Finland. The reported uses are incorporated in exposure-based prioritization metrics.
High Priority Chemicals Data System	Product Testing Data reported to the States of Washington and Oregon by Product Manufacturers
Washington State Product Testing Database	Product Testing Data conducted by Washington State Department of Ecology

Through the literature survey, CPSC staff will review completed assessments and database sources to determine where best to focus a search for more in-depth information. The PECO statement is a central part of the analysis plan for the subsequent literature search. A PECO statement stands for population, exposure, comparison, and outcome. The PECO statement describes which studies will be included or excluded, based on class-specific scope questions. PECO statements can be informed by readily available information, such as completed assessments and database sources. PECO statements are also informed by CPSC's statutory authority and regulatory coverage. For example, PECO statements for class-specific risk assessments would generally focus on human exposure related to consumer products. The hazard endpoints and exposure metrics are described in PECO statements.

An analysis plan details the process in which CPSC staff plans to look for technical information related to risk assessment for chemical substance(s) within a class. The literature search is completed after a literature survey, is informed by the PECO statement, and can be broad or narrow in scope. A broad literature search, for example, would retrieve any record from bibliographic data (*i.e.*, PubMed, Web of Science, and Google Scholar) related to the chemical substance(s) or chemical class of interest. For example, CPSC staff could consider all human health toxicological endpoints, all potential source and exposure pathways, and all potential risks to any human of any age. A narrow literature search would add additional discipline-specific keywords and/or rely on forward searching key data sources identified during the literature survey. The literature search plan shows how the PECO statement is used to inform criteria that describe which studies are identified as relevant and included for use in the risk assessment. For

example, CPSC staff could consider one key toxicological endpoint, for one age group or sex, through a more-targeted subset of potential exposure pathways.

An analysis plan also details the process for how CPSC staff plans to identify relevant data sources related to risk assessment for chemical substance(s) within a class. Data sources could be relevant to human health hazard assessment, exposure assessment, or both. Relevancy is informed by the inclusion/exclusion criteria which are described in class-specific PECO statements.

Hazard Data evidence mapping

A hazard data evidence map presents the number and type of studies that have been identified in the literature survey for different hazard endpoints. The data evidence map shows which types of data (animal toxicity, human studies, human epidemiology, and new approach methodology) are available across different hazard endpoints. The data evidence map, along with prior knowledge of the likely toxicity of a class given its structure and biological activity, informs which endpoint(s) will be targeted for future data gathering in support of risk assessment.

Exposure Assessment Conceptual model

A conceptual model provides a visual aid showing how different potential sources may lead to exposure in different populations of interest. Sources will be described as different kinds of consumer products or different microenvironments, such as home or school. Background sources unlikely to be directly associated with consumer product sources will also be described. Exposure pathways describe how chemical substances are transported from a source to a receptor (consumer) through different media. Receptors include different subpopulations, such as different age groups and sexes, will be described. Finally, a cross-reference to potential effects (based on literature survey) for these receptors will be presented. When all of this information is shown together, it forms the basis of an exposure assessment through development of exposure scenarios.

Market Use Profile

A market use profile describes where and how OFRs are used. The following data elements are typically included within market and use profiles:

- Production volume trends for the chemical(s) of interest:
    - Domestic manufacture of the chemical substance(s)
    - Importation of the chemical substance(s)
- Industrial sectors where OFRs have been used over time:
    - Processes used to formulate OFRs for different end-use applications,
    - Importation as part of a mixture or finished article,
- End-use applications where OFRs have been used over time:
    - Product-use category,
    - Functional-use category,
    - Material type category,

- End-of-life considerations:
    - Reuse and recycling
    - Disposal

CPSC staff plans to focus on consumer uses where products are used in or around residences and schools, consistent with CPSC's regulatory authority. This broader look at a chemical substance(s) market use profile will provide a mechanism to show:

- which chemical classes are used in which consumer products,
- which chemical substances are no longer manufactured or imported, and when this occurred,
- which chemical substances are not used in consumer product applications,
- which chemical substances are used solely as a flame retardant, and which have other functional uses, and
- trends associated with the above, coupled with regulatory history to inform where potential uses in consumer product applications may still occur into the future.

Risk Assessment

Literature Searching, Screening, and Bibliography

Following development of a literature search plan, staff will conduct the literature search of the primary scientific literature using bibliographic databases such as PubMed, Web of Science, and Google Scholar. It is likely that the number of records retrieved from class-specific literature searches will be high (hundreds to thousands). CPSC staff plans to use specialized tools to manage records. These tools provide mechanisms to de-duplicate data sources, automate screening, identify related studies, and prioritize studies for data extraction and evaluation. The final product of a literature search is a bibliography of relevant data sources. Relevant data sources are studies that meet inclusion criteria described in the PECO statement. Some data sources may fit within the PECO statement, but are otherwise unable to proceed past screening because, for example, there is no English version of the data source or there is no full-text readily available. The final product of the literature search is a bibliography containing relevant data sources which could be used in class-specific risk assessments.

Data extraction and evaluation

Following identification of relevant data sources, staff will extract data from these data sources. CPSC staff plans to use specialized tools to extract data. These tools provide mechanisms to extract core data and relevant contextual details. Data extraction is a time-intensive process. Data evaluation means reviewing each data source based on pre-defined acceptability criteria. These criteria vary based on the hazard and exposure data type. Acceptability criteria ensure that data are reliable for use in risk assessment. CPSC staff plans to use specialized tools to evaluate data. These tools provide mechanisms to evaluate data based on answers to pre-defined questions. Data evaluation is a time-intensive process. CPSC staff plans to use an iterative process for data extraction and data evaluation. CPSC staff plans to tier both evaluation and extraction to ensure that relatively more resources are used to consider key data

sources for the risk assessment. First-tier evaluation may involve targeted review for availability of needed data elements. First-tier extraction may involve targeted identification of which specific kinds of data are available for chemicals within a class. First-tier extraction and evaluation may be used to prioritize which studies are fully extracted and evaluated if there are many (hundreds) relevant studies for a class-based risk assessment. Full extraction includes identifying and organizing specified elements for each selected study, including chemical name and other identifiers, study design, details of the animal model or population studied, doses, toxicity endpoints, study results, statistical methods, and other study details. Full evaluation considers data quality, data sufficiency, data consistency, and data relevance for purposes of using the information in the risk assessment.

Data integration

Data integration is the process used to array toxicity and exposure information. Integration can be accomplished in several ways, based on how much and which types of data are available. Due to the diverse nature of the OFR classes, different approaches for data integration can be considered, based on the data available. The final step of data integration is to select toxicity and exposure values to use in risk characterization.

Tiering and Iterating Within a Risk Assessment

CPSC staff plans to tier consideration of hazards, exposures, and risks. In this way, CPSC staff plans to iterate derivation of acceptable daily intake or unit risk values, exposure doses, and risk characterization values many times. This iteration will be informed by available empirical data, relevance and availability of predictive models, and resource availability. First-tier calculations are generally conservative point-estimates based on readily available data, while second- and-later tier calculations are generally distributions based on a more complete consideration of available data.[4]

Hazard identification and dose-response assessment may be tiered based on the data available, where the tiers require increasingly complete, detailed, and quantitative data across the chemical subclass. The level of refinement is related to data availability and the level of complexity presented in the assessment. Staff anticipates that data sufficient for hazard assessment are available for some of the OFR subclasses, although data may only be available for some members of a subclass. In the cases that comprehensive, traditional, laboratory animal-based toxicity data will not be readily available for all identified substances in all OFR classes, CPSC staff will need to consider the use of other types of data, such as data generated using methods that generally fall under the new approach methodologies (NAMs) to fill data gaps for the data-poor members of a class.

Exposure Assessment can be tiered based on the data available. The level of refinement is related to data availability and the level of complexity presented in the assessment. Modeling of exposure can be completed with minimal inputs, but is associated with uncertainty if those inputs are not rooted in empirical evidence. Review and/or generation of product testing data informs exposure estimates by providing empirical, rather than estimated, levels of chemical emission or

[4] Embry, Michelle R., et al. (2014). Risk assessment in the 21st century: roadmap and matrix. Critical Reviews in Toxicology 44.sup3: 6-16.

migration of OFRs from consumer products. Review and analysis of exposure estimates reported by others and environmental and biomonitoring data provide more robust evidence of exposure but takes time to evaluate and integrate. CPSC staff plans to iterate its exposure assessment of class-based OFRs based on the data available.

The risk characterization step of a risk assessment can be tiered, based on the data available for the hazard assessment and exposure assessment steps, as described above. CPSC staff will also have to determine the type and quantity of data necessary to attain the confidence needed to draw risk-based conclusions. If CPSC requires certain empirical hazard or exposure data on each chemical in a subclass, the cost and time implications are substantial.

Example of First-Tier Hazard Identification

For the case that an OFR class has only a few well-studied members, staff may use one or a combination of approaches to characterize the toxicological effects and adverse health outcomes associated with the class. Staff could use a small number of well-studied chemicals to represent the toxicology of the entire class, or apply computational methods to use existing information to quantitatively predict health outcomes for the class. These methods would avoid performing new laboratory research. Similarly, for dose-response information, staff could use existing published hazard values (*e.g.*, EPA reference doses) for one or more subclass members, if relevant and appropriate, in conjunction with toxicokinetic or other data, to inform the range of the hazard values for a subclass.

Example of Second-Tier Hazard Identification

If more extensive data are needed before staff can proceed with hazard and dose-response assessments for OFR subclasses, staff may need to sponsor new NAM research, as well as the more traditional toxicity testing with laboratory animals. Time requirements for toxicity research generally are measured in years, and costs can be significant. In this case, the subclass would be deferred until new data are available.

When sufficient dose-response data are available, staff will use the toxicological point-of-departure information from existing studies and reviews to calculate hazard values (*i.e.*, acceptable daily intake (ADI) and cancer unit risk). Comprehensive dose-response analyses, beyond using only published data analyses and hazard values, will require staff to complete evaluations of available studies for chemicals in each subclass, select appropriate data for analyses, and conduct quantitative assessments and modeling to derive hazard values for each subclass. The steps of literature searching, and evaluating and compiling existing data and published hazard values, are common to both tier 1 and tier 2 hazard identification and dose-response analyses processes.

Example of First-Tier Exposure Assessment

For the case where an OFR class has multiple diverse uses and limited empirical data, CPSC staff can model exposure, based on physicochemical properties, reported use information, and market research that informs how people interact with products containing these OFRs. Exposure scenarios are internally consistent, but other evidence streams (environmental monitoring, biomonitoring, or doses or concentrations reported by others) are considered only to the extent that they change the overall magnitude of estimated exposures.

Example of second-tier Exposure Assessment

If an OFR class has narrow uses and some class members have robust empirical data, CPSC staff will evaluate available exposure information (*i.e*., environmental monitoring, biomonitoring, or doses or concentrations reported by others) and use this information to flag where additional product testing and consumer exposure modeling can refine exposure assessments. New product testing (emission and migration) can be completed for multiple class members, where existing data are not available, and all class-members will be subject to exposure modeling estimates.

Example of First-Tier Risk Characterization

One approach to risk characterization with limited resources and limited data availability is to start with readily available information, in conjunction with health-protective assumptions (*i.e*., worst-case), to characterize a scenario before moving to higher-tier analyses with more data- and labor-intensive refinements in the analyses. This approach can be part of a process to identify if the level of estimated risk indicates that no further action is necessary (*i.e*., low risk), or if the estimated risk requires further analyses in support of possible risk management actions (*i.e*., high risk).

A first-tier risk characterization would include minimal characterization of uncertainties or variability in the parameters and analyses, relying instead on the most readily available hazard and exposure data, and qualitative discussion of the sources and extent of uncertainty and variability. Similarly, evaluation of potentially affected populations would rely on simplified assumptions about potentially exposed populations.

Example of Second-Tier Risk Characterization

Second-tier risk characterization could involve consideration of uncertainty and variability through more complex, quantitative analyses of ranges of numeric information from the hazard identification and dose-response assessments, and from the exposure assessment. The risk characterization would also include more robust evaluations of the potentially exposed populations, as well as trends in exposure and risk.

Risk Characterization and Cumulative Risk Assessment

Risk characterization is the part of a risk assessment that estimates the potential occurrence of health effects under specified conditions of exposure. It may include characterization of affected populations, as well as characterization of uncertainties and variability. CPSC staff generally characterizes non-cancer risks using a hazard index approach.[5] A hazard index greater than one is considered to indicate a potential risk of adverse health effects. For cancer, an individual lifetime excess risk greater than one per million is the default level of concern, which may trigger labeling or other action.[6] An important part of risk characterization is to describe the variability, uncertainty, and limitations of the risk assessment. A class-based assessment requires a description of any assumptions or methodologies used for the class approach.

[5] Ibid., CPSC 1992.
[6] The Commission determines on a case-by-case basis whether action is needed to reduce a hazard.

Another consideration of class-based risk assessment is the possibility of interactions when individuals are simultaneously exposed to members of the same class. If class members act by a similar mode of action, or have a common health endpoint, it is reasonable to consider whether there are additive, synergistic, or antagonistic effects, such as with phthalates.[7] Staff will evaluate the potential for mixture or cumulative effects following established guidelines.[8, 9, 10]

Generation of New Hazard Data

As part of the CPSC-sponsored project, NASEM staff provided an overview of the potential costs of toxicology tests that may be needed to fill data gaps and resolve discordant data, reproduced in Table C3 below.[11]

Table C3: Toxicology Study Costs*

Traditional Methods (Approximate Costs)	
14-day rodent study, two species with pathology	$70,000–$90,000
90-day rodent study, two species, both sexes with pathology	$1–1.3M
2-year chronic rodent study, two species, both sexes with pathology	$3.5–4M
28-day immunotoxicity, one species both sexes	$100,000
Teratology, two species	$200,000
New Approach Methodologies (approximate Costs)	
Zebrafish, with or without intact chorion	$6,000–8,000
C. elegans	$500
ToxCast, about 275 cell-based and 75 biochemical assays	$30,000
*Costs are for a single chemical. Costs are estimates for general comparison purposes. Actual costs depend on many factors of study design and performance. Analytical chemistry, data handling, and quality assurance costs are not included in these estimates.	

[7] Chronic Hazard Advisory Panel (CHAP) (2014) Report to the U.S. Consumer Product Safety Commission by the Chronic Hazard Advisory Panel on Phthalates and Phthalate Alternatives. U.S. Consumer Product Safety Commission, Bethesda, MD. July 2014. Available at: http://www.cpsc.gov/chap.

[8] EPA (2000) Supplementary Guidance for Conducting Health Risk Assessment of Chemical Mixtures. Risk Assessment Forum, U.S. Environmental Protection Agency, Washington, DC 20460. August 2000. EPA/630/R-00/002. http://ofmpub.epa.gov/eims/eimscomm.getfile?p_download_id=4486

[9] ATSDR (2004) Guidance Manual for the Assessment of Joint Toxic Action of Chemical Mixtures. May 2004. In: U.S. Department of Health and Human Services PHS, Agency for Toxic Substances and Disease Registry, Division of Toxicology (ed). U.S. Department of Health and Human Services, Atlanta, GA.

[10] NRC (2008) Phthalates and Cumulative Risk Assessment. The Task Ahead. Committee on the Health Risks of Phthalates, National Research Council, National Academy Press, Washington, DC.

[11] Letter from Gregory H. Symmes, Executive Director, Division of Earth and Life Studies, The National Academies of Sciences, Engineering, and Medicine, to Kristina Hatlelid, U.S. Consumer Product Safety Commission. April 4, 2019.

CPSC rarely funds toxicology studies directly because most toxicology tests are quite expensive. The primary options are to nominate chemicals for testing to the National Toxicology Program (NTP) or to work through EPA's Interagency Testing Committee (ITC). The staff envisions nominating chemicals for in vitro or short-term in vivo tests, in part, due to the length of time and cost of performing tests for chronic health endpoints, such as carcinogenicity or reproductive toxicity. A two-year carcinogenicity study costs approximately $4M and takes 10 years to complete; much of the time is used for range-finding studies before the study and pathology studies following the completion of the "in-life" portion of the study.

Generation of New Exposure Data

Exposure data from the literature from bibliographic databases, and from sources such as government agencies, academic institutions, and other organizations (sometimes called "gray literature") has been developed for a variety of reasons. This heterogeneity means that while the data was fit-for-the original study author's purpose, it may not directly answer CPSC staff's questions on specific exposure pathways of interest for consumer products containing OFR chemicals. CPSC staff may consider additional fit-for-purpose emissions testing and/or migration testing. These tests are designed to answer specific questions about the magnitude and rate of emissions and/or migration from OFR sources into air, surfaces, dust, or biological media over time.

Unlike toxicity studies, exposure studies are generally less expensive and do not require years to conduct. Exposure studies can be done in-house in the CPSC laboratories, through interagency agreements with other federal laboratories, or through contractors.

Table C4: Product testing to inform Exposure Study Costs*

Chamber test (large chamber), characterize emissions, sorption, influence of temperature, source air characteristics	$200,000
Chamber test (small chamber), characterize emissions, sorption, influence of temperature	$160,000
Chamber test (micro chamber), characterize emissions, influence of temperature	$80,000
Tailor chamber tests for SVOC chemicals,[12] measure properties such as y^o, K, and D[13]	Variable

[12] ASTM 2017. Standard Guide for Selecting Volatile Organic Compounds (VOCs) and Semi-Volatile Organic Compounds (SVOCs) Emission Testing Methods to Determine Emission Parameters for Modeling of Indoor Environments.

[13] The chemical concentration in the air phase immediately above the material surface is given by y^o. Material-air partition coefficient, K, is the ratio of chemical concentrations in the solid and air phases when the chemical is in equilibrium across the interface between the two phases; it is a highly sensitive variable when modeling SVOCs.

Migration to saliva-dynamic chamber head over heels, migration of chemical from product to saliva over time	$60,000
Migration to surrogate skin, migration of chemical from product to surrogate skin over time	$50,000
Chemical content, Source Characterization	$5,000

*Assumes sample size of 10 products and targeted analysis for known chemicals. Costs are estimates for general comparison purposes. Actual costs depend on many factors of study design and performance. Analytical chemistry, data handling, and quality assurance costs are not included in these estimates.

Diffusion coefficient, D, is the diffusion constant for the chemical in the bulk material (resistance to movement through the material).

TAB D: Preliminary Profile of the OFR Chemical Market

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A
B

D

DATA SOURCES OF THE OFR CHEMICAL MARKETS

This Tab provides a review data sources for obtaining information from the market for OFR chemicals and describes where and how OFRs are used. This information is needed for the exposure assessment step of the risk assessment. This Tab identifies the 14 subclasses of OFRs that will be assessed; describes how we conducted this review; and identifies several sources of information on the market and use of these chemicals.

The Subclasses of OFRs to Be Assessed

Following the recommendation of the National Academy of Sciences, Engineering, and Medicine (NASEM), rather than conducting a risk assessment of all OFRs as a class, CPSC staff believes it will be more effective to divide the OFR chemicals into subclasses and conduct risk assessments on each subclass. NASEM published its report titled, "A Class Approach to Hazard Assessment of Organohalogen Flame Retardants," in May 2019. The report inventories 161 Organohalogen Flame Retardants (OFRs) and classifies them into 14 subclasses. Appendix B of the report, page 59, presents a table of these 161 OFR chemicals, listed by NASEM-defined subclasses. This breakdown of OFR chemicals by subclass is shown as table D-1 (on the next page) and includes the number of chemicals in each subclass and their Chemical Abstracts Service (CAS) numbers.

Chemical Market Review Process

There are many sources of information on the OFR chemical's market. This section identifies some. It provides a discussion of the OFR market datasets, their sources, periodicity, and any data limitations. As part of the class-based approach of review, staff will identify the market uses of OFR chemicals and the consumer products that contain them. This section includes examples of data that may be used for an OFR Chemical Market Review, based on data currently available for the NASEM-defined OFR chemical subclasses.

When beginning an OFR Chemical Market Review, there are three main steps to the search:

Step 1: Obtain the Chemical Abstracts Service Registry Numbers (CAS RN) for each chemical in the OFR chemical subclass, the alternative chemical names, chemical abbreviations, and the chemical formulas for each chemical within the subclass.

Step 2: Use the CAS RN (or CAS No.) to search for available use, volume, and price data for the chemicals in the subclass. Note the availability of data on consumer products and substitutes.

Step 3: Identify market characteristics of OFR chemicals within the defined subclass, including domestic manufacturing and import practices.

Table D-1. Fourteen OFR Subclasses Formulated on the Basis of Chemotypes and Predicted Biologic Activity

OFR Subclass	No. Chemicals	CAS No. of Chemicals
Polyhalogenated alicycles	17	25495-98-1; 25637-99-4; 3194-55-6; 3194-57-8; 134237-50-6; 134237-51-7; 134237-52-8; 678970-17-7; 678970-16-6; 678970-15-5; 169102-57-2; 138257-19-9; 138257-18-8; 3322-93-8; 77-47-4; 87-84-3; 1837-91-8
Polyhalogenated aliphatic carboxylate	4	3066-70-4; 5445-17-0; 5445-19-2; 19660-16-3
Polyhalogenated aliphatic chains	12	52434-59-0; 1522-92-5; 3296-90-0; 3234-02-4; 96-13-9; 109678-33-3; 85535-84-8; 71011-12-6; 85535-85-9; 63449-39-8; 75-95-6; 79-27-6
Polyhalogenated benzene alicycles	4	1084889-51-9; 893843-07-7; 1025956-65-3; 155613-93-7
Polyhalogenated benzene aliphatics and functionalized	19	168434-45-5; 23488-38-2; 39569-21-6; 87-83-2; 85-22-3; 38521-51-6; 58495-09-3; 31780-26-4; 84852-53-9; 497107-13-8; 59447-55-1; 34571-16-9*; 855993-01-0*; 855992-98-2*; 147-82-0; 57011-47-9; 61368-34-1; 93-52-7; 39568-99-5
Polyhalogenated benzenes	19	608-90-2; 87-82-1; 84303-46-8; 60044-26-0; 67733-52-2; 67889-00-3; 69278-62-2; 59080-40-9; 13654-09-6; 36355-01-8; 92-66-0; 92-86-4; 115245-07-3; 60044-24-8; 59080-37-4; 77102-82-0; 16400-50-3; 67888-96-4; 59080-39-6
Polyhalogenated bisphenol aliphatics and functionalized	11	66710-97-2; 55205-38-4; 37853-61-5; 37419-42-4; 3072-84-2; 33798-02-6; 79-94-7; 25327-89-3; 21850-44-2; 4162-45-2; 79-95-8
Polyhalogenated carbocycles	15	13560-89-9; 51936-55-1; 13560-92-4; 34571-16-9*; 855993-01-0*; 855992-98-2*; 2385-85-5; 18300-04-4; 115-28-6; 1773-89-3; 1770-80-5; 115-27-5; 31107-44-5; 40703-79-5; 52907-07-0
Polyhalogenated diphenyl ethers	12	1163-19-5; 32534-81-9; 60348-60-9; 32536-52-0; 58965-66-5; 5436-43-1; 207122-16-5; 189084-67-1; 41318-75-6; 189084-64-8; 68631-49-2; 207122-15-4
Polyhalogenated organophosphates	22	114955-21-4*; 1373346-90-7*; 126-72-7; 19186-97-1; 115-96-8; 13674-84-5; 13674-87-8; 38051-10-4; 66108-37-0; 78-43-3; 6145-73-9; 33125-86-9; 49690-63-3; 7046-64-2; 5412-25-9; 53461-82-8; 61090-89-9; 140-08-9; 6749-73-1; 4351-70-6; 6294-34-4; 115-98-0
Polyhalogenated phenol derivatives	7	118-79-6; 608-71-9; 615-58-7; 42757-55-1; 39635-79-5; 70156-79-5; 25713-60-4*
Polyhalogenated phenol-aliphatic ethers	9	3278-89-5; 31977-87-4; 35109-60-5; 37853-59-1; 61262-53-1; 3555-11-1; 607-99-8; 26762-91-4; 20217-01-0
Polyhalogenated phthalates/benzoates/imides	11	32588-76-4; 183658-27-7; 90075-91-5; 82001-21-6; 20566-35-2; 26040-51-7; 7415-86-3; 55481-60-2; 632-79-1; 117-08-8; 57011-47-9
Polyhalogenated triazines	6	52434-90-9; 57829-89-7; 75795-16-3; 25713-60-4*; 114955-21-4*; 1373346-90-7*

*An asterisk indicates that the chemical occurs in more than one category.

Sources of information on OFR chemicals are outlined in Tab C. Publicly available data on OFR chemicals used in consumer products are available from the U.S. EPA and from state agencies. Intergovernmental organizations, like the Commission for Environmental Cooperation (CEC) and international organizations like the European Chemicals Agency (ECHA) provide information in a global context. Here are a few example datasets that will be used in depth:

- U.S. EPA Chemical Data Reporting (CDR) database
- North American Agreement on Environmental Cooperation (NAAEC), Commission for Environmental Cooperation (CEC)
- High Priority Chemicals Data System (HPCDS), Interstates Chemicals Clearing House
- European Union Chemical Agency (ECHA), Registration, Authorization and Restriction of Chemicals (REACH)
- Alibaba and other online price databases

This tab provides a more complete picture of where OFR chemicals are used in consumer products, OFR chemical volumes, and current OFR chemical prices. The OFR chemicals market is global and the data reported in this section draw on worldwide data sources. Although CPSC staff will consider additional information during the class-based risk assessment, this in-depth look at data currently available for OFR chemicals can help to inform the planning and review process.

Following the structure defined under the NASEM report of 161 OFR chemicals, in 14 subclasses, staff presents current OFR chemical market use data in summary tables. Substantial data are available for some OFR chemicals from various sources, although there are some gaps in the available data for some OFR chemicals.

The petition submitted to CPSC in 2015, specified four product categories that contain OFRs: (1) infant, toddler, or children's products; (2) upholstered furniture; (3) mattresses; and (4) electronic casings. As available, staff presents current market-use data for these products.

Consumer Uses of OFR Chemicals

Although there are other potential uses of OFR chemicals for other functions, OFR chemicals are mainly used for their flame retardant properties.[1] Most of the OFR chemicals reported to the 2016 CDR were reported for industrial functional use as a *Flame Retardant*.

The Organization of Economic Co-operation and Development (OECD) recently harmonized functional use definitions, which were later codified in updated CDR 2020 rulemaking. The OECD defines "flame retardants" as:

> Chemical substances that alter the normal degradation or combustion processes of plastics, rubbers, textiles, papers and woods, etc. Used on the surface of or incorporated into combustible materials to reduce or eliminate their tendency to ignite when exposed to heat or

[1] Industrial functional use for eight OFR chemicals in the CDR database were not disclosed, were labeled as Confidential Business Information (CBI), or were classified as "Not known or reasonably ascertainable."

a flame for a short period of time. Used to raise the ignition point; and/or to slow down or prevent combustion.[2]

CPSC staff will consider multiple data sources that describe functional use, including regulatory reporting, voluntary reporting, literature, or modeled estimates.[3]

U.S. EPA Chemical Data Reporting

The Chemical Data Reporting (CDR) rule, issued under the Toxic Substances Control Act (TSCA), requires manufacturers (including importers) to give the U.S. Environmental Protection Agency (EPA) information on the chemicals they produce domestically or import into the United States. It is the most comprehensive source of basic exposure-related information on chemicals in commerce. EPA makes the non-confidential market and use data available to the public in the ChemView database. The most recent data available from the CDR is for the 2016 reporting year. The 2016 CDR data contain information on industrial processing and use of chemical substances, including chemical-specific industrial function, the geographic locations of industrial sites, and intended consumer (or commercial) use of the chemical products. The 2016 data reports industrial function, while 2020 and later cycles of CDR are expected to report functional use more generally, for industrial function, commercial, or consumer applications.[4]

The current CDR data provide manufacturing, processing, and use data for 30 OFR chemicals defined in the NASEM report, from 11 of the 14 defined OFR subclasses.[5] In the database, data are withheld where values are masked to protect Confidential Business Information (CBI) claims, or are currently undergoing a CBI substantiation process. The CDR summary table below provides an overview of OFR chemicals organized into 14 OFR subclasses defined by NASEM and the count of OFR chemicals reported in the CDR dataset. (See table D-2.) Although only 30 OFR chemicals are reported in use (from the 161 defined OFR chemicals), data for the majority of OFR chemical subclasses are available (11 of the 14 subclasses).

Table D-2. CDR Summary

OFR subclasses CAS No.	**No. of Chemicals in subclass**	**Number in CDR data**
1 - Polyhalogenated alicycles CAS No. 25637-99-4; 3194-55-6; 77-47-4	**17**	**3**
2 - Polyhalogenated aliphatic carboxylate	**4**	**0**
3 - Polyhalogenated aliphatic chain CAS No. 3296-90-0; 63449-39-8	**12**	**2**
4 - Polyhalogenated benzene alicycles	**4**	**0**
5 - Polyhalogenated benzene aliphatics and functionalized CAS No. 84852-53-9	**19**	**1**

[2] OECD 2017. Internationally Harmonised Functional, Product, and Article Use Categories. Available at: http://www.oecd.org/officialdocuments/publicdisplaydocumentpdf/?cote=env/jm/mono(2017)14&doclanguage=en

[3] Phillips, K. A., Wambaugh, J. F., Grulke, C. M., Dionisio, K. L., & Isaacs, K. K. (2017). High-throughput screening of chemicals as functional substitutes using structure-based classification models. *Green Chemistry*, *19*(4), 1063-1074.

[4] https://www.epa.gov/chemical-data-reporting

[5] The initial 2016 CDR data contain information on chemical substances manufactured (and imported) for the year 2015.

6 - Polyhalogenated benzenes	**19**	**0**
7 - Polyhalogenated bisphenol aliphatics and functionalized CAS No. 79-94-7; 25327-89-3; 21850-44-2; 4162-45-2	**11**	**4**
8 - Polyhalogenated carbocycles CAS No. 13560-89-9; 115-27-5	**15**	**2**
9 - Polyhalogenated diphenyl ethers CAS No. 1163-19-5	**12**	**1**
10 - Polyhalogenated organophosphates CAS No. 19186-97-1; 115-96-8; 13674-84-5; 13674-87-8; 38051-10-4; 6294-34-4	**22**	**6**
11 - Polyhalogenated phenol-aliphatic ethers CAS No. 3278-89-5	**9**	**1**
12 - Polyhalogenated phenol derivatives CAS No. 118-79-6; 42757-55-1; 25713-60-4*	**7**	**3**
13 - Polyhalogenated phthalates-benzoates-imides CAS No. 32588-76-4; 183658-27-7; 20566-35-2; 26040-51-7; 632-79-1; 117-08-8	**11**	**6**
14 - Polyhalogenated triazines CAS No. 25713-60-4*	**6**	**1**
Total count of OFR chemicals (duplicates)	**161**	**30**

* An asterisk indicates that the chemical occurs in more than one category.
Source: Table B-2 of A Class Approach to Hazard Assessment of Organohalogen Flame retardants (2019), joined to CDR reporting data (2016).

Commercial and Consumer Use

The CDR database tracks the commercial and consumer uses of chemicals. The following table lists products that contain OFR chemicals used for their flame retardant properties in commercial and consumer products, as reported in the CDR. (See table D-3.)

Table D-3. OFR Chemical Commercial and Consumer Use Product Categories

Commercial and Consumer Use Product Categories: Flame Retardants
Adhesives and sealants
Batteries
Building/construction materials - wood and engineered wood products
Building/construction materials not covered elsewhere
CBI*
Electrical and electronic products
Fabric, textile, and leather products not covered elsewhere
Flame retardant
Foam seating and bedding products
Intermediate for agricultural (pesticides and fungicides)
Paints and coatings
Plastic and rubber products not covered elsewhere

*Data claimed as Confidential Business Information.

The CDR data indicate whether the reported chemical was used in products intended for children. According to the 2016 CDR, only four OFR chemicals are manufactured (or imported) for use in children's products.[6] (See table D-4.) The four OFR chemicals reported for use in children's products were used for their flame-retardant properties. The end use of these products fell into the following product use categories: (1) electrical and electronic products, (2) foam seating and bedding products, (3) building/construction materials not covered elsewhere, and (4) fabric, textile, and leather products not covered elsewhere.

Data for children's products are available from other sources described later in this section.

Table D-4. OFRs Used in Children's Products, by Subclass, CDR 2016

Polyhalogenated benzene aliphatics and functionalize
Domestically Manufactured
Decabromodiphenylethane (CAS No. 84852-53-9)
Polyhalogenated bisphenol aliphatics and functionalized
Domestically Manufactured
Tetrabromobisphenol A (CAS No. 79-94-7) (TBBPA)
Imported
Tetrabromobisphenol A (CAS No. 79-94-7) (TBBPA)
Polyhalogenated phthalates-benzoates-imides
Domestically Manufactured
2-Ethylhexyl 2,3,4,5-Tetrabromobenzoate (CAS No. 183658-27-7)
Bis(2-ethylhexyl) tetrabromophthalate (CAS No. 26040-51-7)

Note: Not included in this table are those chemicals where amounts in children's products are reported as "Not known or reasonably ascertainable."

Although the CDR provides information about domestic manufacturing and importation of chemicals, the sources of the data are limited to manufacturers and importers of chemicals on the TSCA–Toxic Substances Control Act–Inventory. Manufacturers do not necessarily know all end-uses of their chemicals. Self-reporting by industry is also limited to inventories that reach or exceed a given threshold at any given site during the calendar year. Some data are withheld and Confidential Business Information is suppressed from public disclosure, leaving an incomplete profile of OFR chemical use in the United States. More importantly, many consumer products are imported. Information on imported products is not included in the CDR.

As noted, CPSC staff will consider past and future CDR reporting. The next CDR reporting period concludes in 2020, during which new information for manufacture and import occurring in 2016–2019 will be reported to EPA. CPSC staff will also consider the expanded use information available from the 2020 CDR, as well as other reported information on OFR chemicals that become available.

[6] Many responses in the field for 2015 Product Use Intended for Children were left blank. Four OFR chemicals, not listed here, responded "Not known or reasonably ascertainable."

Commission for Environmental Cooperation

The Commission for Environmental Cooperation (CEC) is an intergovernmental organization structured under the North American Agreement on Environmental Cooperation (NAAEC). The CEC is comprised of three member states, Canada, Mexico, and the United States, to support cooperation among the NAFTA partners to address environmental challenges and opportunities presented by continent-wide free trade.

In a report published in 2015, on the uses of manufactured products that contain flame retardants, 16 selected flame retardants were reviewed using publicly available data to find their prevalence in North American markets and their uses in manufactured items.[7] Of the 16 flame retardants reviewed, 11 are OFR chemicals identified by the 2019 NASEM report on Organohalogen Flame Retardants. (See table D-5.)

Although data are not available for every OFR subclass, the table provides a helpful introduction to some of the terminology used by industry in the fabrication of goods that contain OFR chemicals and an outline of which consumer products are known to contain them. For example, polyurethane foams, or PUFs, are widely used by industry to make flexible products like seat cushions and mattresses, or rigid products like picnic coolers, foam insulation, or coatings for wood products. Industrial chemical producers will typically make custom formulas for their customers that consist of a polyol that determines the physical properties of the PUF and will usually contain other inputs, including flame retardants. Other terms like high-impact polystyrene (HIPS), and EPS foam (expanded polystyrene) and XPS foam (extruded polystyrene) are used in the description of intermediate goods and manufactured items. EPS and XPS foam are used in insulation.

Table D-5. OFR Chemical End Uses, by Subclass

CAS No.	Abbreviation	Intermediate Goods and Manufactured Items
Polyhalogenated alicycles		
25637-99-4 and 3194-55-6	HBCD	Plastics: XPS/EPS, HIPS, latex. PUF: insulation board. Paints and coatings. Wallpaper. Textiles (upholstery). Printed wiring boards, electrical and electronic components (TVs, laptops) (identified in electronic waste, though conflicting sources indicate HBCD is not used in electronic casings for TV sets and computers.
Polyhalogenated benzene aliphatics and functionalized		
84852-53-9	DBDPE	PUF: car seats, changing table pads, portable mattress, rocking chairs, couches, and stuffed toys. Rubber and plastics. DBDPE is currently the most abundant FR used in High-Impact Polystyrene (HIPS). Coatings. Textiles, including tent fabric. Car interiors. Electrical components, such as computers, TVs, and electrical appliances.
Polyhalogenated organophosphates		

[7] CEC. 2015. *Enhancing Trilateral Understanding of Flame Retardants and Their Use in Manufactured Items: Supply Chain Analysis of Selected Flame Retardants Contained in Manufactured Items that are used in Indoor Environments*. Montreal, Canada: Commission for Environmental Cooperation. 33pp.

13674-84-5 and 6145-73-9	TCPP	PUF: upholstery, bedding, nursing pillow, changing pad, car seat, portable crib, glider rocker, portable mattress, footstool, headrest from chair, chair, ottoman. Rigid PUF: building insulation and refrigerator casings. Wallpaper. Can also be used in isocyanurate PUF, PVC, EVA and phenolics, and epoxy resin.
13674-87-8	TDCPP	PUF: car seat head supports, car seat insets, high chair pad headrests, baby walkers, baby carriers, changing pads, sleeping wedges, bassinet mattresses, car seats, portable crib mattresses, infant bath slings, booster seats, nursing pillows, couches, chairs, sofa beds. Textiles, specifically tent fabric. Wallpaper. LCD TV components; laptop components.
Polyhalogenated phenol-aliphatic ethers		
37853-59-1	TBE	Plastics: ABS, polycarbonate, and HIPS. Hard and soft plastic toys. Electric and electronic equipment. Construction materials (sealant around window frames, other consumer adhesives).
Polyhalogenated phthalates/benzoates/imides		
183658-27-7	TBB	PUF: car seats, changing table pads, portable mattresses, couches, rocking chairs.
20566-35-2	No abbreviation.	Rigid PUF; RIM, elastomers; coatings adhesive and fibers as PHT4-DIOL [specific end products not identified].
Polyhalogenated phthalates/benzoates/imides		
26040-51-7	TBPH	PUF: couches, car seats, changing table pads, portable mattresses, rocking chair, furniture. PVC: imitation leather. Ethylene propylene diene terpolymer (EPDM): wire and cable. Textiles; carpet backing, coated fabrics, wall coverings. Electrical and electronic products. Rubber and plastic products, including thermoplastic polyurethane (TPU), styrene butadiene rubber (SBR), and neoprene. Sealants/adhesives, building and construction.

Source: Report 11638, CEC.
Note, TBE is the chemical abbreviation for OFR chemical 1,1'-[Ethane-1,2-diylbis(oxy)]bis[2,4,6- tribromobenzene]; or 1,2-bis(2,4,6-tribromophenoxy) ethane. All other chemical abbreviations are defined elsewhere in this tab.

The petition CPSC received in 2015, from consumer organizations, medical associations, and organizations representing workers and firefighters, requested that the Commission ban the use of flame retardants in residential upholstered furniture, among other products. According to reports published by the CEC, one of the primary uses for flexible PUF is from the home furnishings industry.[8] Residential upholstered furniture is assembled with pre-cut polyurethane foam and upholstery components that are likely to contain flame retardants. To fabricate flexible PUF into cushions used in residential upholstered furniture, PUF is manufactured in bulk as foam cushioning and is sent to cushion cutters, who trim the cushions to end-user specifications. Trimmed cushions are then sold to end-use manufacturers for incorporation into the final home furnishing product.[9]

[8] Ibid.
[9] Industry representatives estimated that approximately 30 percent of residential upholstered furniture is imported from overseas, predominantly from China.

Excess flexible PUF trimmings are known to be recycled in large quantities. At the end of Tab D, general lifecycle considerations of OFR chemical contamination from recycling practices are discussed further.

High Priority Chemicals Data System

The High Priority Chemicals Data System (HPCDS) by the Interstates Chemicals Clearing House provides data reported to states by manufacturers of children's products.[10] The 2015 petition requested that the Commission ban the use of flame retardants in durable infant or toddler products, children's toys, child care articles, or other children's products. Staff plans to use this dataset and others to identify concentrations of OFR chemicals present in children's products.

The HPCDS provides public access to consumer product information reported by companies. Responsible manufacturers (and importers) self-report to the system, if their products contain chemicals of high concern. As an example, select data available from this dataset are presented in Table D-6 and are organized by NASEM subclass.

Table D-6. HPCDS OFR Chemicals Reported in Children's Products, by Subclass

NASEM Subclass: Polyhalogenated alicycles		
Chemical	CAS No	Products
Hexabromocyclododecane (HBCD)	25637-99-4	• Fancy Dress Accessories** • Indoor/Outdoor Games*
NASEM Subclass: Polyhalogenated aliphatic chains		
Chemical	CAS No	Products
Short-chain chlorinated paraffins (SCCP)	85535-84-8	• Artists Accessories • Artists Painting/Drawing Supplies Other* • Arts/Crafts Variety Packs* • Baby Carrier* • Baby Hygiene/Grooming Other* • Bath/Pool Water Toys* • Blankets/Throws • Board Games/Cards/Puzzles – Accessories/Replacement Parts* • Board Games/Cards Puzzles Other* • Clothing Accessories Variety Packs* • Dolls/Soft Toys (Non Powered) • Dresses • Handwear* • Headwear* • Measuring/Geometric Equipment (Stationary)* • Musical Toys Other* • Overalls/Bodysuits* • Pants/Briefs/Undershorts* • Role Play – Housekeeping/Gardening/DIY Toys* • Shirts/Blouses/Polo Shirts/ T-shirts* • Skirts*

[10] The Interstates Chemical Clearing House is used by two states: Oregon and Washington.

		• Toys/Games – Other • Toys/Games Variety Packs
NASEM Subclass: Polyhalogenated benzene aliphatics and functionalized		
Chemical	CAS No	Products
Decabromodiphenyl ethane (DBDPE)	84852-53-9	• Baby Safety Protection (Non Powered) ** • Occasion Supplies Other ** • Overalls/Bodysuits* • Pants/Briefs/Undershorts* • Shirts/Blouses/Polo Shirts/T-shirts* • Skirts*
NASEM Subclass: Polyhalogenated bisphenol aliphatics and functionalized		
Chemical	CAS No	Products
Tetrabromobisphenol A (TBBPA)	79-94-7	• Musical Toys Other* • Occasion Supplies Variety Packs* • Personal Accessories Variety Packs* • Sleepwear Variety Packs • Socks* • Toys/Games – Other ** • Toys/Games Variety Packs
NASEM Subclass: Polyhalogenated diphenyl ethers		
Chemical	CAS No	Products
Decabromodiphenyl ether (BDE-209) (decaBDE)	1163-19-5	• Socks* • Toys/Games – Other* • Toys/Games Variety Packs
NASEM Subclass: Polyhalogenated organophosphates		
Chemical	CAS No	Products
Tris(2-chloroethyl) phosphate (TCEP)	115-96-8	• Shirts/Blouses/Polo Shirts/T-shirts **
Tris (1-chloro-2-propyl) phosphate (TCPP)	13674-84-5	• Arts/Crafts Variety Packs** • Fancy Dress Costumes/Accessories Variety Packs** • Toys/Games – Other** • Toys/Games Variety Packs*
Tris(1,3-dichloro-2- propyl)phosphate (TDCPP)	13674-87-8	• Headwear ** • Outdoor Play Structures** • Toys/Games – Other **
Bis (chloromethyl)propane-1,3-diyl tetrakis-(2- chloroethyl) bis(phosphate) (V6)	38051-10-4	• Shoes – General Purpose* • Toys/Games Variety Packs*
NASEM Subclass: Polyhalogenated phthalates/benzoates/imides		
Chemical	CAS No	Products
2-ethylhexyl-2,3,4,5-tetrabromobenzoate (TBB)	183658-27-7	• Bath/Pool Water Toys* • Overalls/Bodysuits* • Pants/Briefs/Undershorts* • Shirts/Blouses/Polo Shirts/T-shirts* • Skirts*
Bis (2-ethylhexyl) tetrabromophthalate (TBPH)	26040-51-7	• Overalls/Bodysuits • Pants/Briefs/Undershorts* • Shirts/Blouses/Polo Shirts/T-shirts • Skirts*

Source: http://theic2.org/hpcds, accessed February 2020.

* Indicates the substance use has no chemical function, but may be a contaminant within the product.
** Indicates use as flame retardant.

According to data available from February 2020, the HPCDS dataset provides data for 11 of the 161 NASEM-defined OFR chemicals from seven of the 14 subclasses. Although the dataset provides helpful information regarding the presence of OFR chemicals in children's products, this list should not be considered exhaustive. The reporting triggers for the HPCDS are not health-based values and do not correspond to existing safety standards or laws.[11] As mentioned in Tab C, product testing data are also available from the Washington State Department of Ecology and other data sources, which staff will consider.

KEY SOURCES OF DATA ON OFR VOLUMES

Manufacture and use of certain OFRs has declined due to voluntary phase-outs, state laws, or international standards related to "mounting evidence that many flame retardants are associated with adverse human health effects."[12] Nonetheless, production volumes of other OFRs have remained constant over time and "emerging" flame retardants are known to have been developed as substitutes for older or restricted flame retardants. CPSC staff will evaluate data on production volumes of chemicals available from a variety of data sources. This section presents information on production volumes of OFR chemicals defined in the NASEM report, compiled from various trusted data sources.

Chemical Volumes Reported in the CDR

EPA's CDR rule under the TSCA requires manufacturers (including importers) to provide information on chemical volumes. These data include annual aggregate amounts of chemical for the preceding 4 years, reporting the volume of chemical manufactured or imported into the United States to a site.[13] EPA uses these data to help assess potential human health and environmental impacts of the reported chemicals.

As part of a class-based approach, CPSC staff will consider the rank-order for chemicals with highest to lowest production volume and the rank-order for chemicals with the highest to lowest percent of production volume used in consumer products. This data can be evaluated chemical-by-chemical or by class for a single CDR cycle or over multiple CDR cycles. Data from the 2016 CDR, for example, show aggregate production volumes are reported for 11 of the 14 NASEM-defined subclasses. For the years 2012 through 2015, volume data are available for 18 OFR chemicals, while production volume data were withheld for at least 11 OFR chemicals, from seven NASEM-defined chemical subclasses. Volumes for OFR chemicals were not reported for the polyhalogenated aliphatic carboxylate, benzene alicycles, or benzenes subclasses. Withheld values are a limitation of the CDR data source, and staff will need to identify alternative data sources for complete reporting on OFR chemical volumes. Noted previously, the next CDR reporting period concludes in 2020, during which data for the 2016-2019 period will be reported.

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[11] The presence of a chemical in a children's product does not necessarily mean that product is harmful to human health.

[12] National Academies of Sciences, Engineering, and Medicine 2019. *A Class Approach to Hazard Assessment of Organohalogen Flame Retardants*. Washington, DC: The National Academies Press. https://doi.org/10.17226/25412.

[13] Companies are required to retain records that document any CDR information reported to EPA for at least 5 years.

Although OFR chemical volumes are reported for individual chemicals, as part of a class-based approach, staff will consider volumes of chemical by OFR chemical class. Looking at the data by NASEM-defined OFR subclass provides a different perspective on aggregate OFR chemical quantities. Ranking the OFR subclasses by volume high to low, according to 2015 reported volumes, we find that the largest amounts of OFR chemicals come from the (1) organophosphates, (2) aliphatic chain, (3) bisphenol aliphatics and functionalized, and (4) benzene aliphatics and functionalized subclasses.[14]

Table D-7. CDR total volume by OFR subclass, ranked largest to smallest, 2015

Volume Rank	OFR subclass
1	Polyhalogenated organophosphates*
2	Polyhalogenated aliphatic chain
3	Polyhalogenated bisphenol aliphatics and functionalized*
4	Polyhalogenated benzene aliphatics and functionalized
5	Polyhalogenated phthalates/benzoates/imides*
6	Polyhalogenated alicycles
7	Polyhalogenated carbocycles*
8	Polyhalogenated phenol derivatives*
9	Polyhalogenated diphenyl ethers
10	Polyhalogenated phenol aliphatic ethers*
11	Polyhalogenated triazines*

* Indicates volume data withheld from subclass total.

The European Chemicals Agency

The European Chemicals Agency (ECHA) maintains a database of information through the Registration, Authorization and Restriction of Chemicals (REACH) regulation, which was enacted in 2007, to improve the protection of human health from risks posed by chemicals.[15] Staff plans to use data from this extensive resource. ECHA's REACH regulation applies to consumer products, such as chemical cleaners and disinfectants, paints, articles of clothing, furniture, and electrical appliances, as well as to the chemicals industry. Various datasets will be useful from this agency.

REACH has established procedures for collecting and assessing information on chemicals and hazardous substances, with the goals of improved safety and the understanding of the chemicals industry in Europe. Companies are required to register any toxic or hazardous substances with the agency, and ECHA receives and compiles the data made available from the registrations. CPSC staff plans to directly consider primary studies identified from the completed assessments by ECHA, as noted in Tab C. For reference, detailed data available currently by the ECHA and REACH assessments are presented in this section, organized by NASEM-defined subclass, as an example.

[14] Note, data are withheld for 11 OFR chemicals, in 7 OFR subclasses.
[15] ECHA provides a hazard database, noted previously in Tab C, table C1.

In the most recent REACH registration, on May 31, 2018, 5,435 companies submitted 33,363 registrations of various substances to ECHA. Registrations were received from 28 EU Member States and three European Economic Area countries, with the largest share coming from Germany (26 percent). Of the thousands of registrations submitted, data for at least 37 unique OFR chemicals are currently available in the dataset, from 12 of the NASEM-defined subclasses.

From the data available, the top four OFR subclasses, by volume, are the same in Europe (2017 data) and the United States (2015 data). The polyhalogenated bisphenol aliphatics and functionalized subclass is the second largest OFR subclass, by volume, as reported through ECHA. Recall that it was the third largest, by volume, as reported in the CDR, although data were withheld.

The volumes reported in the CDR and REACH data are similar, to an extent. In both the E.U. and U.S. markets, no chemicals from the Polyhalogenated benzene alicycles or Polyhalogenated benzenes subclasses were reported. And while a chemical from the Polyhalogenated aliphatic carboxylate subclass was reported in the REACH database and not in the CDR, the chemical had no reported use in finished products.[16] Proportional volumes of OFR chemicals aggregated by OFR subclass in the United States and European Union are comparable. (See table D-8.)

Table D-8. Annual volume by OFR subclass, ranked largest to smallest

CDR Rank	REACH Rank	OFR subclass
2	1	Polyhalogenated aliphatic chains*
3	2	Polyhalogenated bisphenol aliphatics and functionalized
4	3	Polyhalogenated benzene aliphatics and functionalized
1	4	Polyhalogenated organophosphates
7	5	Polyhalogenated carbocycles
6	6	Polyhalogenated alicycles*
9	7	Polyhalogenated diphenyl ethers
5	8	Polyhalogenated phthalates/benzoates/imides
8	9	Polyhalogenated phenol derivatives
11	10	Polyhalogenated triazines
10	11	Polyhalogenated phenol aliphatic ethers
	12	Polyhalogenated aliphatic carboxylate*

* Indicates volume data withheld from subclass total.

Toxic OFR Chemical Accumulation

According to the ECHA dataset, there is broad consensus by scientists that at least seven OFR chemicals from five NASEM-defined subclasses are either persistent, bioaccumulative, toxic (PBT), carcinogenic (C), skin sensitizing (Ss), toxic to reproduction (R), or respiratory sensitizing (Sr). Another 15 OFR chemicals defined in the NASEM report have some or mounting evidence of such properties. Currently, only two chemicals are being considered for

[16] Methyl 2-bromohexanoate is reportedly used only as an intermediate.

their possible endocrine-disrupting (ED) properties. They are also considered possibly PBT. Both of these OFR chemicals fall within the polyhalogenated bisphenol aliphatics and functionalized subclass.

The only NASEM-defined subclasses that do not include chemicals for which warnings are available are the polyhalogenated benzene alicycles, and polyhalogenated benzenes subclasses. Staff will consider available data for the 23 OFR chemicals for which there are ECHA warnings.

Staff expects the REACH dataset available from ECHA to provide additional information. Domestic and international organizations require additional reporting of market, use, or exposure information for certain chemicals that meet predefined criteria. These criteria may include chemicals that meet production volume thresholds, are designated as PBT, have been identified as persistent organic pollutants (POPs), or have existing assessments or designations that characterize toxic effects. When chemical substances appear on these lists, they may have additional reported information. CPSC staff will consider information available on OFR chemicals (and their analogs) from chemicals on these lists, including when they were added and why they were added.

For example, under the REACH framework, The European Commission has aimed to place all currently known "substances of very high concern" on a candidate list by 2020. A "substance of very high concern" is defined as one that is carcinogenic, mutagenic, and toxic for reproduction, or persistent, bioaccumulative, or toxic to the environment. When a chemical is declared a "substance of very high concern" under REACH, it signals to industry that this substance should eventually be phased out of the market and companies are encouraged to look for safer alternatives. Staff will review data collected under the REACH framework for OFR chemicals of high concern.

Nine OFR chemicals from five OFR subclasses, as defined in the NASEM report, are REACH candidates, and have been flagged as substances of very high concern, listed in table D-9. Although table D-9 is an informative example, it should not be considered a complete list of hazardous OFR chemicals. Other organizations have identified OFR chemical hazards, and staff plans to review OFR chemicals present on multiple lists.[17]

Table D-9. REACH OFR chemicals of very high concern

CAS No.	Name	2015 CDR reported volume	2017 REACH reported volume	HPCDS – Children's Products	For Sale by TCI America[1]
Polyhalogenated alicycles					
25637-99-4	Hexabromocyclododecane	1,000,000 - 10,000,000 lb	1,000 – 10,000 tonnes per annum	Yes	No
3194-55-6	1,2,5,6,9,10-Hexabromocyclododecane	1,000,000 - 10,000,000 lb	—	No	Yes
134237-50-6	alpha-Hexabromocyclododecane	—	—	No	No
134237-51-7	beta-Hexabromocyclododecane	—	—	No	No

[17] Flame retardants were identified as a priority group by HBM4EU in 2016, and were categorized for inclusion in EU-biomonitoring based on data availability.

134237-52-8	gamma-Hexabromocyclododecane	—	—	No	No
Polyhalogenated aliphatic chains					
85535-84-8	Alkanes, C10-13, chloro	—	0 - 10 tonnes per annum	Yes	No
Polyhalogenated carbocycles					
13560-89-9	Dechlorane plus	Withheld	100 – 1,000 tonnes per annum	No	No
Polyhalogenated diphenyl ethers					
1163-19-5	Bis(pentabromophenyl) ether (decaBDE)	< 25,000 lb	1,000 – 10,000 tonnes per annum	Yes	No
Polyhalogenated organophosphates					
115-96-8	Tris(2-chloroethyl) phosphate	25,000 - 100,000 lb	0 - 10 tonnes per annum	Yes	Yes

[1]Chemicals for sale were also marked in stock by retailer, available to ship as of March 2020.

OFR CHEMICAL PRICE SOURCES

Chemical price data are not published in any government dataset, and prices will fluctuate according to market conditions. In this section, current market prices of various OFR chemicals available for purchase are summarized according to NASEM-defined subclass, as an example of the limited data available. Just as OFR chemicals have a variety of uses, OFR chemicals vary in price. The selected price data presented in this section provide a snapshot of pricing from March-April 2020, but cannot represent the extent of prices available in the OFR chemicals market. Staff notes that pricing information is variable over time and can be impacted by global economic conditions.

Distributors of chemicals supply OFRs to customers in the United States for various industrial uses. These chemical distributors should be divided into at least two separate categories: small-scale and bulk-scale distributors. Small-scale distributors typically sell chemicals by the gram (g), while bulk-scale distributors sell chemicals by the kilogram (kg) or metric ton.

Small-scale distributors keep stocks of chemicals supplied in domestic locations in the United States and have them on hand, ready to ship to customers in small amounts. Although small-scale distributors should be able to supply the needs of customers quickly, they are limited in the amount (or volume) of chemical they are able to provide to a customer. Bulk-scale distributors operate somewhat differently to serve the need for larger quantities of chemical.

Bulk-scale distributors and suppliers typically require a minimum order of 1kg of chemical, but depending on the supplier, and the chemical ordered, the minimum quantity of chemical required for an order may vary.[18,19] Prices for bulk-scale OFR chemical orders are typically listed as price ranges, to allow for negotiation between parties on quantity, packaging, storage, lead times, international delivery, and other relevant considerations.[20] Furthermore, bulk-sale

[18] The primary source used for price information on bulk-scale OFR chemical distribution referenced here is Alibaba.com. The site is a global wholesale trade database that provides information on a large array of products.
[19] The minimum order for TCPP (CAS No. 13674-84-5) is one ton, from Haihang Industry (Jinan) Co., Ltd. Trading. Packaging for delivery is made in 200 kg iron drums.
[20] Many distributors of wholesale OFR chemicals manufacture in China and export internationally.

suppliers often list the maximum supply ability per year (in tons) for potential customers to consider before purchasing from the wholesale supplier.

Typically, bulk-scale distributors of OFR chemicals are not located in the United States. Unfortunately, because bulk-scale prices are listed in prices ranges (which could typically range from $10 to $50 per kg of chemical[21]), it is difficult to estimate with precision the actual prices received for OFR chemicals in bulk.

A review of small-scale and bulk-scale prices confirms that prices for chemicals do vary by OFR subclass and that purchasing chemicals in large volumes from distributors can result in a price discount.[22] For this analysis, price data from a typical small-scale and bulk-scale distributor were compiled from data available on the Internet.[23] Price data from the small-scale distributor were listed in a price per 1g, 5g, 25g, 100g, or 500g amount of chemical. Price data from the bulk-scale distributor were typically listed per kg or by ton, and often as a price range.

[21] The minimum order for TBPC (CAS No. 25713-60-4) is one kilogram, from Haihang Industry (Jinan) Co., Ltd. Trading. Packaging for delivery is made in 25 kg bags. The listed price range for sale is 10 to 50 USD per kg.
[22] Staff were unable to complete an exhaustive search of the OFR chemicals market, therefore information provided should be considered incomplete and no final or definitive conclusions should be drawn from the selection of price data presented. Additionally, some OFR chemicals are not available for wholesale or retail sale and price data are unavailable.
[23] Price data were collected in March-April 2020.

Table D-11. OFR Chemical Prices, by Subclass

OFR Subclass	CAS No.	Small-scale price[1] (per 25g)	Bulk-scale price[2] (per 25kg)	CDR reported demand	ECHA reported demand
Alicycles	3194-55-6¤	$21	$125	Yes	
	1837-91-8	$1,630			
Aliphatic carboxylate	5445-17-0	$20			
	5445-19-2	$18	$138		Yes
	19660-16-3	$204			
Aliphatic chains	1522-92-5	$39	$119		
	3296-90-0	$16	$263	Yes	Yes
	96-13-9	$24			Yes
	63449-39-8		$23	Yes	Yes
	75-95-6	$525			
	79-27-6	$12			
Benzene aliphatics and funct.	23488-38-2	$1,745			
	87-83-2	$37			
	84852-53-9	$27	$313	Yes	Yes
	59447-55-1	$1,800			Yes
	147-82-0	$47			
	93-52-7	$26			
Benzenes	87-82-1	$33			
	92-66-0		$638		
Bisphenol aliphatics and funct.	79-94-7	$26	$188	Yes	Yes
	25327-89-3	$33		Yes	Yes
	21850-44-2	$46	$113	Yes	Yes
	4162-45-2	$35		Yes	
	79-95-8	$67			
Carbocycles	115-28-6	$94			
	115-27-5	$20	$88	Yes	Yes
Diphenyl ethers	1163-19-5¤		$63	Yes	Yes
Organophosphates	115-96-8¤	$19	$4	Yes	Yes
	13674-84-5		$4	Yes	Yes
	13674-87-8	$38		Yes	Yes
	140-08-9	$121			
Phenol derivatives	118-79-6	$17		Yes	Yes
	615-58-7	$42			
	25713-60-4*	$179	$750	Yes	Yes
Phenol-aliphatic ethers	607-99-8	$180			
	20217-01-0	$35			Yes
Phthalates/ benzoates/imides	632-79-1	$600	$125	Yes	Yes
	117-08-8		$325	Yes	Yes
Triazines	52434-90-9	$34			Yes
	25713-60-4*	$179	$750	Yes	Yes

Source: Data available on the internet.

[1] To compare OFR chemicals in a uniform measurement, prices for OFR chemical are summarized as the price per 25g of chemical for small-scale supplies.

[2] For bulk-scale orders, prices are calculated for a 25kg sale and where the price was listed as a range the midpoint of the lowest and highest price was selected.

* An asterisk indicates that the chemical occurs in more than one category.

¤ Indicates chemical classified as substance of very high concern.

From current available data, a small-scale distributor sells 34 types of OFR chemicals from every OFR subclass, except Polyhalogenated benzene alicycles and Polyhalogenated diphenyl ethers.[24,25] These chemicals are available for a wide range of prices, ranging from $12 to $1,800 for 25 grams of chemical. Across OFR subclasses, the average price charged by the small-scale distributor is $230 for 25 grams of OFR chemical. The highest prices were seen the polyhalogenated benzene aliphatics and functionalized and polyhalogenated alicycles subclasses, though lower priced chemicals in those subclasses were available.[26] Low priced OFR chemicals were found in the polyhalogenated aliphatic carboxylate, aliphatic chains, and phenol derivatives subclasses.

A bulk-scale distributor sells 16 types of OFR chemical from every OFR subclass, except polyhalogenated benzene alicycles and polyhalogenated phenol-aliphatic ethers. Bulk-scale OFR chemical prices range from $4 to $750 for 25 kilograms of chemical, and are less expensive than quantities available from small-scale suppliers. Some of the most inexpensive OFR chemicals available are polyhalogenated organophosphates. Across OFR subclasses, the average price charged by the bulk-scale distributor is $205 for 25 kilograms of OFR chemical.

To the extent that demand for an OFR chemical or chemical subclass depends on the market price for that chemical, CPSC staff is aware of relevant price considerations within the OFR chemicals market.

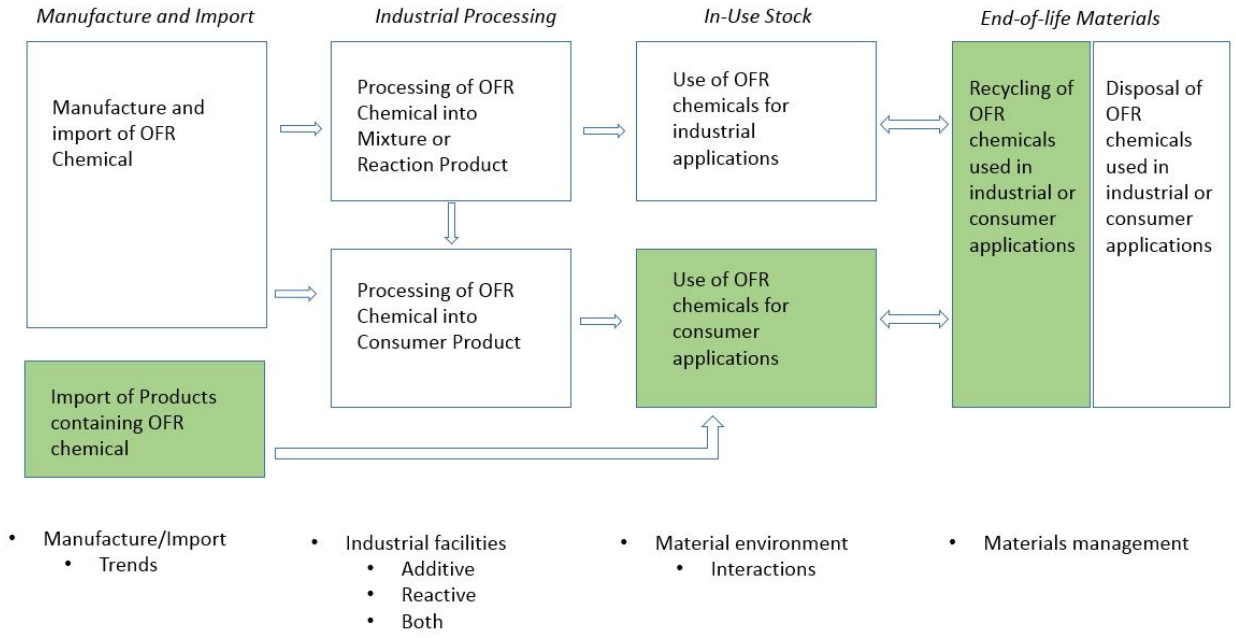
GENERAL LIFECYCLE CONSIDERATIONS

Lifecycle considerations help CPSC staff understand temporal trends and trade-offs across chemical substances used in consumer applications. In 2015, the petitioners argued that consumers are exposed to OFRs because they migrate from the products to the environment no matter how the products are used, and therefore, OFRs pose a risk to consumers. OFR chemical exposure can occur at many points in the life cycle of the flame-retardant chemical; therefore, CPSC staff will take into account lifecycle considerations in assessing OFR chemicals.

The lifecycle of the chemical substance from manufacture to disposal helps contextualize the use of OFR chemicals in consumer products. The product lifetime or product lifespan is the time interval from when a product is sold to when it is discarded. The chemical lifecycle is the time interval from when the chemical is manufactured to when the chemical is discarded. Figure D-1 provides a generic lifecycle diagram that describes this approach.

[24] Almost all of the OFR chemicals are listed as in stock and available for immediate delivery.
[25] Price data for TBPC (CAS No. 25713-60-4) is listed for both the Polyhalogenated Phenol Derivatives and Polyhalogenated Triazines subclasses.
[26] Here, we assume companies that use OFR chemicals as an intermediate good in the production of finished goods to be price sensitive. If two OFR chemicals are available for purchase, and the two chemicals serve an identical purpose (and can be efficiently substituted), we expect an industry preference for the lower-priced chemical.

Figure D-1. Characterizing OFR chemicals in Consumer Applications



Disposal and recycling are considered end-of-life pathways for chemical products and are often considered because the manner in which a product is handled after consumption will contribute to environmental and human-health impacts. For example, octaBDE (CAS No. 32536-52-0) is an OFR chemical that is defined within the NASEM subclass, polyhalogenated diphenyl ethers. Although it is no longer used commercially, in the past, this chemical was used in acrylonitile-butadiene-styrene (ABS) plastic. ABS plastic was used as casing for types of electric and electronic devices, a product category defined in the 2015 petition for both offices and homes.[27]

Today, products that contain octaBDE enter the waste management system in a variety of ways, not in a uniform method. Disposal of goods containing octaBDE is part of the larger topic of electronic waste disposal.[28] The U.S. EPA has identified the recycling and disposal of articles treated with octaBDE as an area of potential concern.[29]

To the extent possible, institutions try to develop hazardous waste policies that balance the conservation of resources with protection of human health. Recycling practices can reintroduce hazardous chemicals into "virgin" materials used to fabricate new consumer products. CPSC staff plans to evaluate the introduction of OFR chemicals into new consumer products as a result of recycling practices.

[27] While the majority of octaBDE chemical is known to have been used in electronic goods, it was also used in TVs, cars, and in building materials.
[28] As mentioned in section 3.D.of this document, the Health Hazard Evaluation Program of the National Institute for Occupational Safety and Health (NIOSH) has assessed occupational exposures to FRs and other substances at facilities, including electronics recycling companies.
[29] Certain Polybrominated Diphenyl ethers; U.S. EPA, Significant New Use Rule. Federal Register Vol.71. 13 June 2006: 34015 – 34021.

TAB E: Glossary

Risk Assessment Terminology

In the context of this project, risk assessment is the scientific process of evaluating the potential adverse health effects of human exposures to toxic chemicals.[1] Risk assessments generally consist of four processes:

- Hazard identification: The determination of whether a particular chemical is or is not causally linked to particular health effects.
- Dose-response assessment: The determination of the relation between the magnitude of exposure and the probability of occurrence of the health effects in question.
- Exposure assessment:[2] The process of estimating or measuring the magnitude, frequency, and duration of exposure to a source and the size and characteristics of the exposed population.
- Risk characterization: The description of the nature and often the magnitude of human risk, including attendant uncertainty.

Terms related to each of these processes are defined below.

Aggregate exposure. The combined exposures to an individual from a single chemical substance across multiple routes and across multiple pathways from multiple sources.

Animal study. Any of a number of types of studies with experimental animals that evaluate toxicological effects of chemicals. In the absence of data from human studies, relevant data from research with experimental animals may be considered in evaluations of harmful effects of chemicals.

Biological activity. Any effect by a chemical in a human or animal or in vitro system. In in vitro systems, potency for biological activity can be described by AC_{50}, which is the concentration that corresponds to 50 percent of the maximum biological activity observed in the assay.

Consumer Products. As defined in the Consumer Product Safety Act,[3] "consumer product" means any article, or component part thereof, produced or distributed (i) for sale to a consumer for use in or around a permanent or temporary household or residence, a school, in recreation, or otherwise, or (ii) for the personal use, consumption or enjoyment of a consumer in or around a permanent or temporary household or residence, a school, in recreation, or otherwise, with exceptions as specified in the Act. 15 U.S.C. § 2052.

Cumulative exposure. The combined exposures to an individual from multiple chemical substances across multiple routes and across multiple pathways from multiple sources.

Cumulative risk assessment. An analysis, characterization, and possible quantification of the combined risks to human health or the environment from multiple agents or stressors.

[1] National Research Council 1983. Risk Assessment in the Federal Government: Managing the Process. Washington, DC: The National Academies Press. https://doi.org/10.17226/366. Available at: http://nap.edu/366.
[2] EPA 2019. Guidelines for Human Exposure Assessment. Available at: https://www.epa.gov/sites/production/files/2020-01/documents/guidelines_for_human_exposure_assessment_final2019.pdf.
[3] Consumer Product Safety Act. Available at: https://www.cpsc.gov/s3fs-public/pdfs/blk_media_cpsa.pdf.

Data-rich chemical. A chemical that is the subject of multiple studies or evaluations, with data from multiple types of studies (*e.g.*, human, animal, NAM) and relevant toxicity endpoints.

Data-poor chemical. A chemical for which no or few published toxicity studies are available, and if studies are available, they are limited.

Dose-response assessment. The quantitative characterization of the relationship between doses or exposure and the occurrence of toxic effects in exposed laboratory animals or human populations.

Exposure pathway. The mode through which one is exposed to a chemical substance, including, but not limited to, food, water, soil, and air.

Exposure receptor. Any person (individual, population, age group, or sex) who is exposed.

Exposure Scenario. The combination of events that define a situation where exposures may occur. Exposure scenarios include a description of sources, pathways, and receptors.

Hazard quotient. The ratio of the estimated exposure to the substance and the level at which no adverse effects are expected. If the hazard quotient is less than 1, then no adverse health effects are expected as a result of exposure. If the hazard quotient is greater than 1, then adverse health effects are possible.

Hazard index is the sum of hazard quotients for two or more substances that have the same toxic effect.

Human study. Any of a number of types of studies, including epidemiology studies, that evaluate the characteristics of exposed and non-exposed human populations for the purpose of detecting harmful effects of specified chemicals or understanding disposition of chemicals in the body.

Imports. Purchases of goods or services by a domestic economy from a foreign economy. In this document, chemical imports refer to purchases made in the United States for chemicals produced in another country.

In silico. Studies conducted or produced using computer modeling or algorithms.

In vitro. Studies performed in a test tube, culture dish, or elsewhere outside a living organism.

In vitro to in vivo extrapolation (IVIVE). The qualitative or quantitative use of in vitro data to define characteristics, such as concentration of a chemical or metabolite in blood, or to predict effects, including toxicity, in animals or humans.

In vivo. Studies in living organisms.

Intermediate goods. Used as inputs in the production of finished goods.

Intermediate chemical. Any chemical substance that is consumed in the manufacturing process of another chemical substance.

In-Use Stock. A product or chemical. The in-use chemical stock is the quantity of chemical on-hand by a firm for use in creating a product. The in-use product stock estimates the quantity of products in use by an individual, household, or population group.

Lifecycle considerations. Used to understand the lifespan of a product. The product lifetime or product lifespan is the time interval from when a product is sold to when it is discarded. The

chemical lifecycle is the time interval from when the chemical is manufactured to when the chemical is discarded.

Manufacture. The mechanical, physical, or chemical transformation of materials or components into new products.

NAM or NAMs. New approach methodologies. A broad description of 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.

Point of departure. A dose that is associated with a specified level of effect for a specific endpoint.

Production Volume. Measures the total amount of substance in a given country produced in a given time period, such as one year. Production volumes reported in the U.S. EPA Chemical Data Reporting (CDR) database include the amount of chemical manufactured plus the amount imported.

QSAR. Quantitative structure-activity relationship. QSAR models are mathematical models for predicting physicochemical, biological, and environmental fate properties of chemicals from information about chemical structures.

Read-Across. An approach in which endpoint information for one chemical (the data-rich source chemical) is used to predict the same endpoint for another chemical (the data-poor target chemical) that is considered to be similar in some way (*e.g.*, structural similarity or the same mode or mechanisms of action). Read-across can be used to assess physicochemical, biological, and environmental fate properties. Read-across approaches require hypotheses, evidence-based justifications, and expert judgment.

Recycling. The process of converting waste into useful material.

Relative Source Contribution. The amount of exposure expected from a single or group of sources for chemical or chemicals of interest compared to aggregate (single chemical) or cumulative (multiple chemicals) exposure.

Risk characterization. The integration of toxicity and exposure information to describe the nature, direction, and magnitude of risks for identified hazard endpoints.

Routes. The particular manner which a chemical substance may contact the body, including absorption via ingestion, inhalation, or dermally (integument). One exposure pathway may result in exposure through multiple routes.

Source. The description of the origin of a chemical substance for purposes of an exposure assessment. Consumer products are primary sources of interest.

Uncertainty. The imperfect knowledge or lack of precise knowledge of the real world either for specific values of interest or in the description of the system.

Unit risk. A measure of excess lifetime cancer risk from exposure to a chemical, expressed as cancer risk per unit of exposure.

Variability. The inherent natural variation, diversity, and heterogeneity across time and/or space or among individuals within a population.

Weight of evidence. Expert consideration of all available data and information, with evaluation of strengths, limitations, and relevance of each study and information source, to determine relative support for hypotheses or answers to questions.