Comments from Earthjustice, Natural Resources Defense Council and Washington Toxics Coalition on Problem Formulation and Initial Assessment Documents for Three Flame Retardant Clusters

Docket IDs: EPA-HQ-OPPT-2015-0068, EPA–HQ–OPPT-2015-0081 and EPA-HQ-OPPT-2014-0730

November 18, 2015

The following comments are submitted by Earthjustice, Natural Resources Defense Council (NRDC) and Washington Toxics Coalition on behalf of our millions of members and online activists. Earthjustice, NRDC, and Washington Toxics Coalition have no financial interest in the chemicals or products that may be the topic of these comments.

We wish to acknowledge and express appreciation for the scientific contributions of experts from outside of our organizations, including Dr. Deborah Rice, Dr. Juleen Lam and Dr. Tracey Woodruff.

EPA opened comment periods for three flame retardant cluster Problem Formulation and Initial Assessment documents, found in the following dockets:
- Chlorinated phosphate ester (CPE; TCEP) cluster flame retardants (EPA-HQ-OPPT-2015-0068)
- Cyclic aliphatic bromides/ hexabromocyclododdecane (HBCD) cluster flame retardants (EPA–HQ–OPPT-2015-0081)
- Tetrabromobisphenol A (TBBPA) and related chemicals cluster flame retardants (EPA-HQ-OPPT-2014-0730)

We commend EPA for undertaking an evaluation of these flame retardant chemical clusters which present significant concerns for adverse effects on human health and the environment. However, we have serious reservations about the approach that the Office of Pollution Prevention and Toxics (OPPT) has outlined. To perform these risk assessments in the manner the public and other regulators expect, and that the Toxic Substances Control Act ("TSCA") requires, OPPT must undertake a systematic review process that takes into account the full range of known exposures, accounts for known data gaps, and considers cumulative risks and exposures faced by people in the real world. We have the following overarching concerns that are relevant to the problem formulations and initial assessments for all three flame retardant clusters, as well as more specific comments on each cluster:

As OPPT acknowledges within the documents, any risk assessment that is based on these problem formulations and initial assessments will underestimate risk. This underestimation is of great concern because such a flawed assessment will lead to misleading and erroneous conclusions about the true risks that these chemicals present. This result would be unacceptable. Consumers, workers, manufacturers, retailers and regulators in both the federal and state governments will rely on EPA's risk assessments to make critical decisions about the continued widespread use of these flame retardant chemicals. The high potential for exposure and hazard that elevated these chemical clusters within the work plan chemical program makes it incumbent upon this Agency not to understate the risk that these chemical clusters pose.

As further detailed in our comments below, incorporation of elements of systematic review would make the process more transparent, ensure that the most appropriate and strongest scientific evidence is used to inform decisions, and aid the public's review, understanding and

ability to comment on each step of the process. **Before finalizing any risk assessments, we believe it is critical that OPPT release separate draft risk assessments for public comment for each cluster**. The Initial Assessment documents do not state how OPPT will use the hazard and exposure data in quantitative risk calculations (for example, which hazard endpoint will be selected to calculate the point of departure). A critical component of the risk assessment process is for the public to weigh in on the assumptions and methodology used to determine the final outcome of these assessments. Therefore, the draft risk assessments for each cluster should be made available for public review and comment.

It is important both for EPA to utilize a transparent process that uses the best available science to inform the final decisions, and for EPA to complete these assessments and move forward with any needed risk mitigation actions in a timely manner. We recommend that the agency set a clear timeline for completion of the public comment periods requested above and for finalization of the risk assessments.

The goal of the work plan chemical program is, as EPA has explained, to identify and assess existing chemicals that have the highest potential for exposure and hazard and if warranted, to subject these chemicals to risk reduction actions under section 6 of TSCA. Given these goals, the risk assessments produced based on EPA's initial assessments must be designed from the outset to satisfy the requirements of a TSCA section 6 rulemaking. To determine if risk reduction actions are warranted under TSCA, EPA will have to assess whether the "manufacture, processing, distribution in commerce, use, or disposal" of chemicals in these flame retardant clusters or *"any combination of such activities*, presents or will present an unreasonable risk of injury to health or the environment."[1] In addition, in order to promulgate a section 6 rule, EPA must "consider and publish a statement" that addresses: "(A) the effects of such substance or mixture on health *and the magnitude of the exposure* of human beings to such substance or mixture, (B) the effects of such substance or mixture on the environment *and the magnitude of the exposure* of the environment to such substance or mixture."[2]

Thus, EPA's risk assessments need to sufficiently account for exposures, including aggregate and cumulative exposures, in order for it to determine whether the "combination of" manufacture, processing, sale, use and disposal of chemicals in these flame retardant clusters present – or will present – an unreasonable risk, and to publish a statement detailing the "magnitude" of human and environmental exposures. A risk assessment that does not take into account the full range of exposures, including an attempt to account for data gaps, cannot fulfill TSCA's requirement that EPA publish a statement of the "magnitude" of the human and environmental exposures.

As this agency is well aware, risk assessment methods have advanced significantly since the early 1990s when EPA last promulgated a section 6 rule, and thus there is no recent TSCA-specific precedent to rely on in ascertaining the risk assessment methods that would be

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[1] 15 U.S. C. § 2605(a) (emphasis added)
[2] *Id.* § 2605(c)(1).

required to support a section 6 rule. Under this circumstance, we believe the Agency might look for guidance to the Federal Insecticide, Fungicide, and Rodenticide Act ("FIFRA"), which also utilizes an "unreasonable risk" standard,[3] and in particular, to the Policy Paper on Revised Risk Assessment Methods for Workers, Children of Workers in Agricultural Fields, and Pesticides with No Food Uses.[4] Under this Policy:

> EPA intends to apply risk assessment techniques developed in implementing the Food Quality Protection Act of 1996 (FQPA) to any pesticide risk assessment, whether it falls under FQPA or not, so long as application of the risk assessment technique is consistent with good scientific practice and is not otherwise prohibited by law. Specifically, this will include:
>   - using an additional safety/uncertainty factor to protect children;
>   - considering aggregate exposures to pesticides from multiple sources;
>   - considering cumulative effects that may occur from exposure to multiple pesticides with a common mechanism of toxicity[5]

In this document, EPA notes that: "Although FIFRA does not require EPA to use these risk assessment approaches in assessing worker risks or non-food use pesticides, FIFRA does require the Agency to consider whether pesticides pose an unreasonable risk. *In assessing risk, EPA believes it should use the best scientific techniques available. Using the FQPA risk assessment approaches for all pesticides is consistent with good science*."[6]

The same reasoning applies here. Because TSCA requires the agency to consider whether chemical substances pose an unreasonable risk, OPPT should use "the best scientific techniques available," and using the approaches listed above for its TSCA work plan chemicals risk assessments – including safety/uncertainty factors to protect children, and considering aggregate exposures and cumulative effects – is, in the Agency's own words, "consistent with good science."[7]

We are providing first our detailed comments that are relevant to all three clusters, followed by the specific comments on each cluster.

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[3] Under FIFRA, to register a pesticide, an applicant must show that the pesticide functions without causing "unreasonable adverse effects on the environment." 7 U.S.C. § 136a(c)(5)(C). FIFRA defines the term "unreasonable adverse effects on the environment" to mean "any unreasonable risk to man or the environment." 7 U.S.C. § 136(bb).

[4] Policy Paper on Revised Risk Assessment Methods for Workers, Children of Workers in Agricultural Fields, and Pesticides with No Food Uses, 74 Fed. Reg. 65,121 (Dec. 9, 2009).

[5] *See* EPA, Revised Methods for Worker Risk Assessment, http://www2.epa.gov/pesticide-science-and-assessing-pesticide-risks/revised-methods-worker-risk-assessment

[6] *Id.* (emphasis added).

[7] *Id*.

DETAILED COMMENTS

1. **The problem formulation and initial assessment should include a systematic review process to conduct a comprehensive literature search, document and evaluate evidence before OPPT determines which exposures and uses it will consider in its assessment.**

A risk assessment is only as robust as the hazard and exposure data on which it relies. Unfortunately, for all three clusters, OPPT has not explained nor documented clearly the process used for researching and reporting hazard and exposure data to support its risk assessments. It appears that the problem formulations and initial assessments are based on a *partial* literature review that does not utilize a systematic approach for evaluating evidence and integrating multiple data streams. Indeed, as we discuss below, we are aware of many relevant studies that OPPT does not appear to have taken into account. Before OPPT drafts its risk assessment documents it must undertake a systematic review to integrate relevant information including human epidemiologic data, *in vivo* toxicological data, *in vitro* cellular and mechanistic data, *in silico* computational information, and data from sampling of environmental matrices and biota.

Systematic review methods for chemical assessments have been developed and implemented through various case studies by the National Toxicology Program (NTP) Office of Health Assessment and Translation (OHAT), the EPA Integrated Risk Information System (IRIS) program, the University of California San Francisco, and others (*see* References 1–5). The National Research Council recently commended the IRIS program on its development of systematic review methods for chemical evaluations (*see* Reference 6). Incorporating a systematic review process would greatly improve the risk assessments overall.

Process
We understand based on meeting with OPPT staff that that the Agency intends to conduct a systematic review as a next step *after* it receives comments on the problem formulations and initial assessments. If this is the Agency's plan we find it to be problematic. First, the Agency has not publicly disclosed this plan anywhere in the published problem formulations and initial assessments or elsewhere on EPA's website. Second, in our view, a systematic review is a critical first step *before* the Agency formulates the problem and conducts an initial assessment. In the absence of a systematic review, OPPT's problem formulations could omit key risks. For example, with the CPE cluster problem formulation, OPPT identified several uses that it believes will not result in significant releases to the environment, and several scenarios that it believes lack sufficient data to quantify risks. But it is premature for OPPT to make these determinations given the limited literature review performed to date. A better approach would be for OPPT to undertake a transparent, rigorous systematic review, integrating multiple data streams regarding chemicals, *before* it determines which exposures and uses it will consider in its assessment.

Undertaking a systematic review before problem formulation would help OPPT ensure that it has identified the proper scope of its assessments. As it stands, the Agency's bifurcated literature review (high level review before problem formulation; systematic review after problem formulation) puts stakeholders and other commenters in a difficult position. It does not make sense for us to devote resources to identify what studies EPA appears to have overlooked (not an easy task since stakeholders are not able to access the body of literature that OPPT is relying on) when OPPT is about to embark on a systematic review. In the future, we believe it would be more efficient, and likely lead to a better result, if OPPT completed and presented its systematic review at the same time that it seeks public input on the problem formulations and initial assessments.

A transparent systematic review of the evidence should begin with a protocol which clearly outlines up-front the study question to be addressed in the assessment, as well as the process for searching, screening, selecting, evaluating, and interpreting the body of scientific literature available. This protocol would increase transparency of both the methods and the process of the assessment, serve as foundation for stakeholders to follow the assessment and provide constructive feedback, as well as allow for better opportunity to engage subject matter experts on the assessment. It also would minimize bias in evidence integration to ensure that inclusion and interpretation of studies does not depend on the study findings and decisions regarding how the evidence will be treated are made prior to seeing the data (*see* Reference 7).

Comprehensive literature search
As soon as possible, we urge OPPT to conduct a systematic review that includes a documented and comprehensive literature search, gathering relevant information from the published, unpublished, and "grey" literature (publicly available government reports, etc.). By documented, we mean that the methodology used to conduct the search (i.e., search terms, which databases were searched, etc.) should be recorded and made available. Because epidemiological studies describe real-world exposure levels, cumulative exposures and relationships that are directly relevant to human health risks, it is critical that the literature search captures epidemiological studies, and that this evidence is integrated to inform decision-making.

Documentation
Upon completing the comprehensive literature search, it is vital for OPPT to also document the results of the search in a way that stakeholders can easily evaluate and access the body of evidence OPPT will rely on for the risk assessment. For instance, EPA IRIS is utilizing the HERO (Health and Environmental Research Online) database to store all references that are used in their assessments. OPPT should also utilize HERO or adopt something similar to transparently document the body of literature that it uses to come to final conclusions.

Evaluation of evidence
OPPT's documentation should include a description of the criteria for study selection. The problem formulations and initial assessments do not reflect any clear, consistent criteria for

including or excluding studies. For example, a comparison of the HBCD cluster document with the IRIS HBCD assessment document reveals numerous studies excluded from OPPT's cluster document. Without information on OPPT's literature search, and inclusion and exclusion criteria, it is impossible to know how and why OPPT selected the studies it chose to include in each cluster assessment. This compromises scientific quality, can introduce bias into the evidence base and subsequent risk assessment, and erode public confidence in the assessment. Ultimately, it undermines the scientific credibility of the final conclusions of the assessments.

OPPT's documentation should also include its criteria for rating study bias, as well as for identifying and potentially excluding very low-quality studies.[8] Evaluation of study bias (internal validity) is a critical step in evaluating the quality of studies. Other agencies and organizations have developed tools specifically designed to evaluate the internal validity of animal toxicology and observational human studies related to environmental health questions (*see* References 1,3–5). OPPT should use EPA's draft *Framework for Incorporating Human Epidemiologic and Incident Data in Health Risk Assessment* which describes criteria and process for assessing epidemiologic studies and integrating this data into a strength of evidence evaluation.

In the absence of criteria for rating the bias and validity of studies, OPPT's study selections for calculating risk estimates and identifying hazards seem scientifically indefensible and arbitrary at best. Ultimately, conclusions should be based on the whole body of literature, potentially excluding the lowest-confidence studies. To do otherwise could lead to biased assessments that are not scientifically supported. As such, the risk assessment could lead to inadequately protective approaches and put public health at risk.

We recommend that OPPT align with NTP, adopting their systematic review process and criteria. These have already undergone significant inter-agency and public review, and are currently being successfully implemented for chemical assessments. Developing systematic review methodology would provide a framework for integrating information from different streams of evidence, including epidemiology studies, animal toxicology and *in vitro*/cellular data into a final concluding statement about the relevance of findings for the study question of interest. Upon completion of a systematic review, OPPT should make any necessary revisions to the problem formulations in light of this review. It should then ensure that the results of this review and any changes to the problem formulations and initial assessments are made available to the public no later than when the draft risk assessments are published for public comment.

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[8] For example, the NTP systematic review framework identifies aspects that would lead to downgrading the confidence rating for studies, including: risk of bias, unexplained inconsistency, indirectness in the relationship between a measured outcome and a health effect, imprecision, and publication bias serious enough to significantly decrease confidence in the body of evidence.

2. The hazard assessments inappropriately overemphasize Good Laboratory Practice (GLP) and guideline studies, show problematic interpretation of data, and do not identify the endpoint to be used in the quantitative risk calculation.

In the absence of clear criteria for study inclusion, it appears that OPPT has determined that all Guideline and GLP-compliant studies will be included in its assessments, even in the face of bias or other weaknesses. GLP is a standard for animal care, data collection and reporting required for industry laboratories in response to fraudulent practices documented in the 1970s. It includes specified approaches to recordkeeping to facilitate audits and reduce fraud. [9] GLP requirements are not necessarily associated with higher quality research, proper study design, or correct statistical analysis (*see* Reference 8). Often, GLP-compliant studies have not undergone scientific peer-review and publication.

As noted by the NAS, GLP criteria fail to address study bias, which is a systematic flaw in the design and conduct of a study that reduces the validity and reliability of the study results (*see* Reference 6 at pp.67-68). Published systematic review case studies have evaluated the risk of bias for GLP studies and found potential biases, demonstrating that following GLP requirements does not necessarily ensure the internal validity of these studies (*see* Reference 9). Furthermore, previous research has shown that an industry funding source influences study outcome (*see* References 10–15). Thus, preferring GLP studies for inclusion is scientifically inappropriate because this would favor industry-sponsored studies and could create a biased evidence base.

Guideline protocols are designed for screening, and do not represent state-of-the-art science. Guideline studies are often designed to identify major toxic effects (apical effects) like cancer and many are insensitive to health endpoints being measured. Guideline studies don't necessarily use modern methods for evaluating chemicals and aren't designed to grapple with the problems of low-dose exposures, behavioral or learning effects, or upstream effects like reduced anogenital distance which are predictors of infertility. Woodruff et al. in 2008 described how upstream consequences of observations in toxicity studies could be used in risk assessment (*see* Reference 16).

OPPT needs to upgrade their approach so that studies are included based on their relevance to the study question, and not on who conducts the study. Failure to include the experimental studies performed by academic or government scientists that have typically undergone extensive peer-review and are aimed at understanding specific scientific questions, would be scientifically inappropriate and indefensible. OPPT needs to define criteria for study inclusion and exclusion, including a risk of bias assessment, to determine the internal validity of each study (similar to what OHAT and Navigation Guide (*see* Reference 4) have done), and separate criteria for determining the quality and strength of the overall body of evidence.

Problematic interpretation of data

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[9] Toxic Substances Control Act (TSCA); Good Laboratory Practice Standards, 54 Fed. Reg. 34,034 (Aug. 17, 1989).

In addition, OPPT's interpretation of the body of evidence is problematic. In places within the problem formulations and initial assessments there seems to be the assumption that results from all studies should be consistent, despite differences in the study design such as the endpoints measured, species tested, and doses evaluated. As we note above, a systematic review process needs to be used to evaluate the literature as a whole, rather than dismissing effects because findings in every study are not identical.

Guideline protocols often specify both male and female study groups because it is well known that males and females may display sexually dimorphic responses. Yet, sometimes OPPT interprets differences in male and female responses to be an indication of inconsistent results, rather than evidence of a sexually-dimorphic response.

The guideline protocol specification of 10 subjects (/sex/dose) is in recognition of the very low power of these studies to detect an effect. Consequently, if no effect is found in studies using fewer than 10 subjects, this cannot be interpreted as evidence that the chemical does not cause the effect in question since the study was not adequately powered to detect any differences. However, if a statistical difference in effect is observed, it suggests that the effect is in fact large, given that the study was underpowered and the difference was still detected. Therefore, as discussed for the interpretation of the Lillienthal et al. study in the TBBPA comments section below, effects found in statistically underpowered studies should not be discounted on this basis.

Endpoint for risk calculation not identified
The problem formulation and initial assessment documents do not identify which hazard endpoint will be used for quantitative risk calculations. As we understand, it is EPA policy to select the most sensitive endpoint for quantitative evaluation in risk assessments in order to ensure adequate health protections for people. The reasoning is that if the evaluation protects against the most sensitive effects, it will also protect against any other adverse effects that might occur at higher levels of exposure.[10]

We recommend that OPPT select the most sensitive endpoint for risk assessment, or else provide detailed rationale for an alternative approach for how the Agency proposes to select the health endpoints for quantitative risk calculations.

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[10] EPA, Off. of Pesticide Programs, Determination of the Appropriate FQPA Safety Factor(s) in Tolerance Assessment 8 (2002). *See also* EPA, Pesticides: Reregistration, Atrazine Updates, Atrazine Evaluation Process, http://archive.epa.gov/pesticides/reregistration/web.old/html/atrazine_update.html ("Reproductive effects are the most sensitive effects observed in atrazine toxicity tests and, as such, our efforts to regulate the pesticide to protect against these effects through drinking water exposure will protect against all other effects that occur at higher levels.")

3. **OPPT should not use a margin of exposure (MOE) approach to evaluate non-cancer risk. OPPT should use the methodology recommended by the National Academies of Sciences (NAS) to harmonize assessment of cancer and non-cancer risk, so that both can be evaluated using a risk-based approach to decision-making.**

The stated intent of OPPT to use a margin of exposure (MOE) approach to evaluating risks in the HBCD (pg. 11) and CPE (pg. 9) assessments is not consistent with current recommendations for approaches that yield the most accurate and useful information for decision-making.

The NAS report *Science and Decisions* (hereinafter "*Science and Decisions*") explicitly states that MOEs are inadequate for comparative risk analysis,[11] and recommends calculations of probabilistic risk distributions using a spectrum of evidence from humans, animals, mechanistic and other relevant studies (*see* Reference 17 at pp.135-9). These probabilistic risk distributions, incorporating variability of responses in the population (including sensitive subpopulations) and any existing uncertainty in the data available, should be used to develop a risk-specific reference dose to quantify the risk associated with a particular level of exposure (*see* Reference 17 at Ch. 5). This will inform the process of risk-based decision making to ensure that risk management decisions are appropriate and based on complete information.

4. **The exposure assessments omit key pathways and analyses that are relevant in the exposed human populations.**

As detailed above, we recommend that OPPT upgrade its scientific evaluation by conducting a systematic literature review and fully documenting its research approach before proceeding with risk assessment. However, we are commenting on the information provided to date while OPPT continues to upgrade its scientific evaluation of the literature for the risk assessment.

Strengths of exposure assessment
The proposal to include consideration for ingestion from dust particles, hand-to-mouth transfer in children, and exposure from drinking water and fish are all appropriate and necessary.

Weaknesses of exposure assessment
a) For all three assessments, OPPT is proposing to consider only oral exposures, without justifying its decision to exclude dermal and inhalation exposure.

    The exclusion of dermal and inhalation exposure is problematic, and even OPPT acknowledges that both these pathways may contribute significantly to human exposure.[12]

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[11] *See also id* at p. 133. ("The end products of noncancer (and nonlinear cancer) assessments in the current paradigm (exposure-effect quotients that qualitatively indicate potential risk—MOEs, RfDs, and RfCs, Figure 5-1) are inadequate for benefit-cost analyses or for comparative risk analyses. MOEs and RfDs as currently defined do not provide a basis for formally quantifying the magnitude of harm at various exposure levels.")

[12] *See, e.g.,* TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Chlorinated Phosphate Ester Cluster Flame Retardants at 9 ("Inhalation exposures and dermal contact are expected to be significant exposure routes for industrial workers and consumers."); TSCA Work Plan Chemical Problem Formulation and Initial

Furthermore, the evidence shows that concentrations in indoor air are high, especially for the CPE cluster chemicals,[13] so failure to include an estimate of inhalation exposure raises serious concern for the accuracy of the assessment.

OPPT notes at pg. 39 (footnote b) of the TBBPA assessment that inhalation and dermal exposure will not be addressed because "TBBPA has a very low vapor pressure" and dermal exposures are "limited." Yet, Fu and Suuberg reported that HBCD has a lower vapor pressure than TBBPA, and the HBCD assessment acknowledges that inhalation exposures do occur (*see* Reference 18). The "available data" that OPPT mentions on pg. 30 suggesting limited dermal uptake are not referenced or provided in the TBBPA document.

Recent research suggests that for some semi-volatile organic compounds (SVOCs) transdermal uptake may be significant via air-to-skin and/ or contact with contaminated surfaces (*see* References 19,20). All the flame retardant chemicals under consideration are SVOCs with the potential for exposure via these dermal pathways, and it is therefore inappropriate to exclude dermal exposures from the assessments without further evaluation. Little et al. developed a model to estimate exposures to SVOCs via gas-phase inhalation, inhalation of contaminated particles, ingestion of contaminated particles, and dermal sorption from the air (*see* Reference 21). This model may be a good starting point for OPPT to obtain more realistic exposure estimates for each of the flame retardant chemicals.

To fully assess the risks to exposed populations, OPPT must consider all potential routes of exposure, using physico-chemical properties and health-protective assumptions where necessary. As recommended in *Science and Decisions,* defaults should be used where science indicates there is a need to quantitatively cover an aspect of the risk assessment but where specific data are lacking (*see* Reference 17, Ch. 6). To not do so would be scientifically inappropriate.

b) Exposure from foods other than fish will not be assessed.

In order to document the magnitude of human and environmental exposures, as TSCA requires, OPPT must attempt to quantify population exposure to flame retardants. This

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Assessment: Cyclic Aliphatic Bromides Cluster Flame Retardants at 24 ("EPA/OPPT considers inhalation and dermal exposure to be important exposure pathways for workers." and pg. 26 "Consumer exposure to HBCD may include inhalation exposure, dermal exposure through direct skin contact with HBCD on the surface of objects or articles, incidental ingestion of inhaled particulates (see 2.4.3), and incidental ingestion of indoor settled dust via hand-to-mouth behaviors."); TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants at 30 ("The general population may be exposed to TBBPA through oral, inhalation or dermal exposure, although aggregate oral exposure is the focus of this assessment.").

[13] TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Chlorinated Phosphate Ester Cluster Flame Retardants at 67 ("The concentrations of phosphate esters in air are several orders of magnitude higher indoors than outdoors").

should include the many foods other than fish contribute to aggregate oral exposures. For example, HBCD is detected in poultry, peanut butter, and canned foods (*see* Reference 22). Especially of concern is the omission of breast milk exposures for infants, a sensitive and vulnerable population. Both the HBCD and CPE documents reference biomonitoring data finding these flame retardants at significant levels in breast milk.

Not including these exposures means they are essentially set at zero, resulting in an **underestimate of exposure**. The fact that EPA cannot regulate other food may have implications for risk mitigation actions, but in no way precludes OPPT from accounting for these exposures in its assessment. In fact, EPA routinely considers exposures from products or sources that it does not regulate in assessments. For example, in its assessment and regulation of the pesticide fumigant sulfuryl fluoride, EPA's Office of Pesticide Programs considered all sources of exposure to fluoride, including ones it did not regulate (such as toothpaste). Considering these exposures was critical for accurate risk calculation and decision making—OPP terminated pesticidal uses of sulfuryl fluoride because children's total exposure to fluoride (mainly from drinking water and toothpaste) exceeded the "risk cup" of acceptable exposure levels.[14]

Similarly, OPPT needs to include exposure from foods other than fish, including breast milk, in the aggregate oral exposure assessment.

c) OPPT inappropriately proposes to exclude certain exposure pathways because, based on limited evaluation, individual risks for those pathways appear to be low.

In both the TBBPA and HBCD documents, OPPT proposes to exclude and not assess certain exposure pathways (such as drinking water) because preliminary calculations or previous assessments indicate low concern/ risk. The major problem with this approach is that such exposures will still contribute to the total aggregate exposure, even if the individual risk of the pathway in isolation is low. OPPT must assess all potential pathways and add those exposures into the aggregate exposure assessment.

d) OPPT gathered information on biomonitoring data and levels in environmental media, but there is no discussion on how these data will be used to estimate exposure.

As the biomonitoring and environmental media data provide useful information on actual, existing, and potential human exposures to flame retardants, OPPT should utilize these data in the risk assessments. OPPT should also include a clear description of the methodology used to do so.

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[14] Sulfuryl Fluoride; Proposed Order Granting Objections to Tolerances and Denying Request for Stay, 76 Fed. Reg. 3422 (Jan. 19, 2011) (Dkt. No. EPA-HQ-OPP-2005-0174).

5. The exposure assessments either omit or do not adequately consider several highly impacted and vulnerable populations, especially with regards to potential cumulative impacts.

Strengths of the exposure assessment
Children are especially vulnerable to flame retardant exposures and toxic effects; the focus on children's exposure via dust ingestion, hand-to-mouth contact, and mouthing of products is necessary and appropriate for all the clusters.

Weaknesses of the exposure assessment
OPPT's consideration of vulnerable and highly impacted populations is inadequate, especially with regards to potential cumulative impacts. These populations include: indigenous communities that rely on traditional foods like fish and marine mammals, other subsistence fishers, workers, and environmental justice communities. The assessments exclude worker and community exposures associated with flame retardant chemical manufacturing and processing, as well as recycling and disposal of products containing flame retardants, despite the fact that these populations potentially face the highest levels of routine exposure. Furthermore, there is no attempt to account for the greater burdens faced by the communities living near chemical manufacturing plants, recycling facilities and incinerators through consideration of cumulative impacts. We provide greater detail below regarding overlooked exposures to workers and environmental justice communities.

a) For the analysis of exposure from fish consumption, only the Chlorinated Phosphate Esters document proposes to obtain accurate information on subsistence fishers.

    The other assessments propose to use inappropriately low values (NHANES data, from participants selected as a "representative population") that do not adequately capture high-end consumption. This is of particular concern for indigenous communities that rely on traditional foods such as fish and marine mammals, and other subsistence fishers.

    All the assessments should use the data on subsistence fishers.

b) Exposures to workers and communities are not adequately considered for the CPE cluster, and exposures related to disposal or recycling of flame retarded products are not being considered for any of the three clusters.

    The CPE assessment will not account for exposures to fenceline communities, manufacturing/ processing workers and non-industrial workers (*see* Conceptual Model for Human Receptors at pg. 30 fig. 2-3 of the CPE document). Monitoring data from the EU shows that these may in fact be some of the most highly impacted populations-- (*see* pg. 23 of the CPE document discussing exposure to CPEs in the air at industrial facilities). Non-industrial workers would include workers installing building insulation (such as spray polyurethane foam), and data from the EU also indicates that building insulation is the

major use of TCPP (*see* Reference 23). We would expect the same is true for the US, but can't be certain as this production volume data is inappropriately claimed as "confidential business information" in the CPE document.

None of the cluster documents propose to account for community or worker exposures related to disposal or recycling of flame retarded products, and only the TBBPA conceptual model even includes recycling as a potential source of exposure. As noted in the TBBPA document, releases from e-waste recycling may be significant,[15] yet exposures to workers and the surrounding communities will not be considered. Releases from disposal of HBCD-containing building insulation may be large and should be considered as a primary source of emissions, especially as more buildings containing such insulation are demolished or refurbished in the future (*see* References 23–25). Workers at facilities where flame retardant-containing products are recycled may have higher exposures; U.S. foam recycling workers have documented higher exposures to PBDEs (*see* Reference 26). This exposure source is especially relevant to the CPE cluster chemicals which are widely used in foam.

Potential exposures workers at manufacturing, processing and recycling facilities should be included in the conceptual models for every cluster, and these exposures accounted for in the assessments. Similarly, potential exposures to communities near chemical manufacturing plants and those near facilities where flame-retarded products are produced, recycled or disposed should be included in the conceptual models for every cluster, and these exposures accounted for in the assessments.

c) Exposures to degradation and combustion products of the flame retardant chemicals will not be considered.

TBBPA can degrade to bisphenol-A (BPA), a chemical with a large toxicity database including epidemiological studies showing adverse health associations. OPPT states that because studies have been conducted with microorganisms collected from TBBPA-contaminated environments, data from these studies cannot be used to predict the rate of TBBPA to BPA degradation in the environment (*see* Appx. C-4-2 at pg. 92 of the TBBPA document). However, it seems that TBBPA-contaminated environments would be the major places that such degradation is occurring, and therefore this is precisely the data that should be used in such a calculation.

Both TBBPA[16] and HBCD (*see* References 27,28) are known to form highly toxic by-products under thermal stress, including polybrominated dibenzo-p-dioxins (PBDDs) and polybrominated dibenzofurans (PBDFs). These by-products can be formed during the

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[15] *See* TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants at pg.43 ("TBBPA concentrations were found in environmental media near e-waste recyclers …and these concentrations could affect the general population living near such facilities.")

[16] Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants pg. 91 "Incineration of TBBPA can result in polybrominated dibenzo-p-dioxins (PBDDs) and polybrominated dibenzofurans (PBDFs) as well as polyaromatic hydrocarbons (PAHs)."

incorporation of flame retardants into products, recycling of flame-retarded products, accidental combustion, and incineration (*see* Reference 28). Firefighters in particular may be highly exposed to PBDDs and PBDFs when flame retarded materials burn in accidental fires (*see* Reference 29).

There is no proposal to assess exposures of communities or certain workers, like those involved in manufacturing or recycling, or firefighters, to toxic by-products. OPPT states that TBBPA's specific contribution to the production of toxic combustion by-products cannot be determined, claiming that there are multiple sources of the same by-products. But since the identity of these combustion by-products is known, the hazards of the products should be assessed and qualitative conclusions drawn about risk. These are unique exposure routes that could result in some very high exposures to workers and neighboring communities; ignoring these exposure scenarios may exclude a significant source of exposure and potential health impacts.

Available data, including data from other countries, should be utilized to account for worker and community exposures to degradation and combustion by-products.

d) There is no proposal to account for cumulative impacts on communities near chemical manufacturing facilities, recycling facilities, or incinerators.

Communities near chemical manufacturing facilities, recycling facilities and incinerators likely bear higher burdens of toxic exposures, including from other chemicals, and poor air quality. This is a major environmental justice issue, yet no proposal has been put forward to account for the disproportionate burden and cumulative exposures these communities likely bear. For example, are TBBPA manufacturing facilities located in areas with significant other environmental quality issues? The *Science and Decisions* report found that failure to evaluate background exposures is a routine, problematic flaw in EPA's risk assessments (*see* Reference 17 at pp. 132-33).

In the absence of data or methodologies to comprehensively evaluate cumulative risks,using tools including indexes, maps, and combined approaches are an important first step in evaluating background exposures and delineating the cumulative context for an assessment (*see* Reference 30). One approach would be to use such data to quantitatively inform variability and vulnerability factors in risk assessments.

6. OPPT cannot ignore known exposures and hazards, even if it cannot readily quantify them. OPPT needs to account for aggregate and cumulative exposures, and should include default values to account for these risks as recommended by the NAS.

When evaluating risk, the available scientific data is often incomplete or very limited. However, data gaps themselves do not indicate a lack of risk—exposures are typically already occurring in the population and adverse health effects may already exist. If they are not quantified, then

these data gaps are treated within risk assessment as if there were no risk. This is scientifically inappropriate. *Science and Decisions* noted that these unstated or implicit assumptions are typically not acknowledged, but can be even more influential than the stated assumptions when accounted for within the assessment of risk (*see* Reference 17 at pp.193-96). The NAS recommended that EPA identify and quantify such implicit assumptions, and use default values to account for them until data are made available. For example, as noted above, OPPT could use available data to develop an exposure model that accounts for inhalation and dermal exposures; existing models for semi-volatile organic chemicals in the indoor environment could be refined (see Reference 21). Where data from other countries is available, it should be used. Furthermore, limited data only hinders the ability to perform a quantitative risk assessment. Using qualitative data from studies, when available, to evaluate risk is a possibility and would be strongly recommended. The bottom line is that OPPT cannot use incomplete data sets as a rationale for failing to account for exposures, hazard or risk; failure to conduct the assessment means continued possible risk to the population.

EPA must use available data to inform the risk assessment, creating models and using clearly stated, health-protective assumptions where needed. If known sources of exposure will not be accounted for, the magnitude of the risk underestimate should be quantified and any risk numbers reported as ranges. Where quantitative evaluation is not possible, qualitative evaluations should still be performed and conclusions drawn as to how risk would be affected.

7. **The strengths of the cluster approach to fill data gaps or perform a cumulative assessment are not utilized. OPPT needs to account for cumulative risks from the multiple chemical exposures within each cluster.**

We agree in concept with OPPT's approach of considering the flame retardant chemicals in clusters and utilizing information across the different chemicals contained within each cluster to evaluate the risk of health effects. However, we disagree with how OPPT has proposed to handle information for each cluster. For the HBCD cluster only 2 of the 3 chemicals proposed will be evaluated, while for the TBBPA cluster only one of the four chemicals proposed will be evaluated.

OPPT stated that read across/QSAR data could not be used to draw quantitative conclusions about multiple chemicals contained within the cluster. While this might be accurate, we believe that qualitative information could still be informative and would help evaluate all of the chemicals contained within each cluster. The criteria used for evaluating cluster chemicals are clearly too narrow because the outcome is that the chemicals contained within the cluster are excluded. This defeats the purpose of evaluating these chemicals in clusters. This functionally is no different from the traditional approach of evaluating one chemical at a time. An even more concerning prospect for these flame retardant chemicals, and industrial chemicals generally, is that the process of regrettable substitution will continue, which is also contrary to EPA's stated goal of reducing health threats from toxic chemicals.

Regrettable substitution is of particular concern for TBBPA, the brominated flame retardant with the highest US and global production volume,[17] for which no other cluster chemical members will be evaluated. OPPT states that "[s]ome limited information is available for the cluster members other than TBBPA. However, EPA/OPPT concluded that no quantitative risk assessment is needed for these other cluster members for one or more of the following reasons: limited information, inability to use the more robust data for TBBPA to read across to other cluster members, low toxicity or likely low risk concerns."[18] We do not believe these reasons are appropriate for concluding that a risk assessment is not **needed**. Although limited information may preclude the Agency from being able to perform a quantitative risk assessment, it is not a basis to conclude that risk assessment is not necessary. This logic also applies to OPPT's rationale regarding its inability to use the robust TBBPA data to read across to other cluster members. Furthermore, OPPT should elaborate on its statement of "likely low risk concerns." How was this determined? Such a determination would typically come from a risk assessment evaluating hazard, exposure, and dose-response. It is unclear how OPPT proposes to make this determination without performing a complete risk assessment. If this is based solely on exposure, this is inappropriate because of the potential for exposure patterns and levels to change over time. Indeed, if any one of the cluster chemicals was used as a replacement for the index/ parent chemicals, we would likely see exposures quickly rise to the level of the index chemical.

Even if data constraints preclude OPPT from performing a quantitative risk assessment, the Agency can and should still undertake a qualitative risk assessment to evaluate what implications potential exposures might have for risk to the exposed population. The potential for health impacts should not be ignored simply because there is a lack of robust data. In fact, qualitative read across was used to support the EU's June 2014 directive limiting TCEP, TDCPP, and TCPP in toys to the lowest detectable levels.[19]

Finally, OPPT needs to account for cumulative risks from the multiple chemical exposures within each cluster. Although information is collected on more than one chemical for the HBCD and CPE clusters, there is no indication that this information will be used to inform consideration of cumulative risk. One way to perform a quantitative cumulative risk assessment is to identify a common endpoint and then make estimates of the relative potency of each chemical. This seems possible for the CPE cluster as there are a number of potential common

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[17] EPA, TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants at 13.

[18] *Id.* at 10.

[19] European Commission, *Commission Directive 2014/79/EU of 20 June 2014 amending Appendix C of Annex II to Directive 2009/48/EC of the European Parliament and of the Council on the safety of toys, as regards TCEP, TCPP and TDCP* (2014), *available at* http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32014L0079&from=EN ("In its opinion SCHER agrees with the conclusion of the alternatives' risk assessments that **there is sufficient information from the structures, physical-chemical properties, toxicokinetics and mutagenic profiles of TCEP, TDCP and TCPP to support a qualitative read-across**, indicating a potential concern for carcinogenicity for TCPP by a non-genotoxic mechanism. The read-across implies, according to SCHER, that considerations given for TCEP could be applied to its halogenated alternatives as well, if used in toy manufacturing."(emphasis added))

endpoints: effects on kidney, cholinesterase inhibition, carcinogenicity, and thyroid function. Furthermore, cumulative exposure information is available in a common matrix, indoor dust, and data indicate that people are co-exposed to CPE cluster chemicals.

In sum, the cluster approach should be used to draw qualitative conclusions where quantitative assessment is not possible. Leaving potential risks of cluster chemicals unaddressed could very likely lead to regrettable substitution. Potential cumulative impacts should be addressed—if not by a full quantitative cumulative risk assessment, at least by quantifying co-exposures and identifying common endpoints.

8. **Confidential business information ("CBI") is inappropriately used to justify non-disclosure, especially in the context of production volume for chemicals that have been on the Inventory for decades, and the identity of manufacturers that are producers of the chemicals in question.**

We are very concerned about the extensive invocation of "CBI" within these problem formulations and initial assessments, which denies the public critical information about these chemical clusters and their uses. Over twenty years ago, an independent review of OPPT's practices revealed that "CBI claims under TSCA are far in excess of what is needed to protect true trade secrets."[20] These problem formulations and initial assessments contain prime examples of CBI claims that do not protect true trade secrets.

To be valid, a CBI claim must comply with TSCA section 14, which requires the information claimed as CBI to meet:

- the criteria for the Freedom of Information Act's (FOIA's) trade secret/CBI exemption and

- EPA's CBI criteria, including that the "business has satisfactorily shown that disclosure of the information is likely to cause substantial harm to the business's competitive position." [21]

We are not persuaded that the information withheld as CBI in these problem formulations and initial assessments meets these criteria.   For example, in the HBCD document (at pp. 17-18, 34, Appx. B) and the CPE document (at pp. 17, 19-21), EPA shields from disclosure national level production and processing volumes of these chemicals. In addition, the assessment of TBBPA withholds the name of one of the manufacturers of TBBPA (p. 20).   How are these pieces of information trade secrets? How could revealing them cause "substantial harm to the business's competitive position"? This inappropriate invocation of CBI is particularly concerning since EPA's claimed inability to rely on the most current production and use volume data will hamper its ability to accurately assess exposures and determine risk. We urge EPA to require the manufacturers to substantiate all information claimed as CBI that EPA would otherwise rely on

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[20] *See* Sheila A. Ferguson et al., EPA, Influence of CBI Requirements on TSCA Implementation 20 (1992) ["1992 Report"], available at http://www.regulations.gov/#!documentDetail;D=EPA-HQ-OPPT-2002-0054-0074
[21] 40 C.F.R. § 2.208(e)(1).

in these assessments. If these data do not meet the substantive criteria to be withheld as CBI, as we doubt they do, they should be included in the draft risk assessments.

CLUSTER-SPECIFIC COMMENTS

The comments below are made without the benefit of well laid out criteria from OPPT for identifying and evaluating the evidence as part of a consistent systematic review approach. As we discuss above, such an approach is critically important. The comments below should be integrated into the protocol we recommend developing for each chemical assessment.

Comments on the CPE cluster

We have several concerns about the risk assessment methods proposed for the CPE cluster.

1. *OPPT must be more robust in its assessment of exposures from inhalation.*

The agency's intentions regarding the inhalation pathway are unclear: the problem formulation states (p. 24) consumers may be exposed through inhalation of both vapor and dust, but then concludes that vapor inhalation will not be addressed due to the lack of route-specific toxicological data. In addition, it does not clarify what information sources will be used to estimate exposure to inhaled dust. A number of studies, including recent personal air sampling in the U.S., have found CPEs associated with airborne particulates. A recent study in Washington State measured both respirable (< 4 µm) and inhalable (> 4 µm) particulates, and found TCPP and TDCPP in both fractions, and TCEP in the inhalable fraction (*see* Reference31), (poster and abstract attached to these comments as Exhibit s 1 and 2, respectively). Given that these compounds are present in small particles that can penetrate deep into the lung, OPPT must assess exposure from inhalation of particulates as well as ingestion of airborne dust.

OPPT must also develop a more robust method for estimating exposure from inhalation of vapor. The agency cites the CPSC 2006 document, which estimates that 98-99% of exposure to TDCPP from furniture foam was via the inhalation route in both adults and children. But OPPT does not discuss how it intends to address this issue. As we note above, ignoring known exposures due to difficulties in quantification will lead to a flawed assessment that underestimates risk.

2. *We are concerned about OPPT's approach to estimating releases to water.*

The agency acknowledges widespread use of TDCPP in textile treatment, but states its intent to assess only TCPP releases from textile finishing without explaining the reason for excluding TDCPP. In addition, while OPPT acknowledges recent research showing down-the-drain releases to water from consumer uses, the agency inexplicably ignores available data on wastewater treatment plant (WWTP) effluent concentrations of CPEs. Some of these data are summarized in Appendix D, and the agency notes that in one study, "[c]oncentrations of chlorinated

phosphate flame-retardants were highest among the chemicals of emerging concern tested."[22] At least two other efforts have analyzed WWTP effluent for CPEs, including a US Geological Survey study that tested effluent from nine WWTPs (*see* Reference 32). Schreder and La Guardia tested effluent from two WWTPs, and found that the estimated contribution from laundry water approximated actual levels found in effluent (*see* Reference 33). They estimated a discharge of 114 kilograms TCPP per year from a single treatment plant, which constitutes a significant source that OPPT cannot ignore.

3. *Data are available that should allow OPPT to estimate exposure via the dermal pathway.*

EPA states that there are data for dermal exposure in rats for TDCPP and human skin for TCPP, and EPA also references a study where nebulized TCEP was quantified.[23] OPPT should incorporate all available information. For example, Canada's estimation of dermal exposure in their assessment may serve as a good starting point for OPPT's analysis.

4. *OPPT should account for cumulative risks from multiple chemical exposures.*

Appendix F ("Human Health Hazard Study Summaries") seems to suggest that there is enough information on toxicity to identify an appropriate endpoint for cumulative risk assessment, yet there is no discussion of how this will be done. It appears that effects on kidney, cholinesterase inhibition, and carcinogenicity, and perhaps effects on thyroid function, can all be modeled in a cumulative risk assessment.[24]

5. *Other comments related to the toxicological data presented.*

OPPT needs to consider that cholinesterase inhibition poses a neurodevelopmental risk. Acetylcholine is critical to brain development and developmental neurotoxicity should be included in the assessment (*see* Reference 34). It must be assumed that a change in neurotransmitter homeostasis represents an adverse effect. In addition, brain lesions and convulsions have also been observed, providing evidence of structural and gross functional effects. There is also a growing body of research using the zebrafish model to assess neurodevelopmental effects of these compounds. Dishaw et al. found that exposure to all three compounds (TDCPP, TCEP, and TCPP) significantly altered larval swimming activity, indicating an effect on neurological development (*see* Reference 35). Oliveri et al. tested TDCPP on zebrafish and found widespread effects over various behavioral assays at doses that could be within the range of human exposures (*see* Reference 36). Oliveri et al. also discuss possible mechanisms based on the effects of organophosphate pesticides, which affect serotonin and dopamine levels (exposure to TDCPP has been found to reduce serotonin and dopamine in zebrafish). OPPT should not dismiss effects on neurological development based on a limited number of

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[22] EPA, TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Chlorinated Phosphate Ester Cluster Flame Retardants at 66, App. D.

[23] *See id.* at 26.

[24] *See id.* at 70-72.

animal studies. A systematic review approach to this literature is needed to accurately and scientifically account for the relationships.

Two points should be considered related to the Moser rodent study: first, righting reflex, motor activity, and other measures in the functional observational battery (FOB) are very crude indicators of nervous system function. A lack of effect on such measures is not necessarily indicative that the brain is not affected. Second, the study did detect effects, inappropriately dismissed by the authors, such as on grip strength, habituation of motor activity, and memory. The authors dismiss the observed effects by pointing out that effects were not observed in other domains, but it should not be expected that every domain/endpoint would be affected. Otherwise, one behavioral test would be sufficient, and the battery used in this study would be unnecessary. The authors' conclusions that the observed effects are not biologically relevant is unwarranted, particularly since, as the authors point out, these are screening tests, which do not tax the behavioral capabilities to a significant degree.

It is unclear why OPPT dismisses potential effects on male reproductive organs, given the results of the two-year bioassay in rats, which is cited in Appendix F of the Problem Formulation and Initial Assessment.[25] The fact that effects were not observed in a different species with a shorter duration of exposure does not negate the findings of the rodent study. Claiming "uncertainty" in the face of the rodent study is improper, and effects on male reproductive organs should be considered in the assessment. Similarly, a number of studies found impairment in thyroid function, including in humans. Thyroid effects must also be considered in the assessment. Again, a prespecified protocol with defined study questions and appropriate approaches for data evaluation would ameliorate these apparent biases in the evaluation of the evidence.

Finally, the CPE Problem Formulation and Initial Assessment indicates TCPP is not likely to partition to the atmosphere,[26] in contrast to recent research finding TCPP among the flame retardants detected in the highest concentrations in the atmosphere (*see* References 37–39). Salamova et al. found ∑OP concentrations in the Great Lakes atmosphere on average at 100 to 1200 times those of PBDEs and Firemaster 550 components. OPPT must do a more thorough review of this literature to adequately assess exposure and environmental impacts.

Comments on the TBBPA cluster
Comments on the exposure assessment
In the TBBPA Problem Formulation and Initial Assessment, dermal, inhalation, and other potential exposure pathways are not depicted in OPPT's conceptual model diagram.[27] As we comment above, OPPT has not provided sufficient data or rationale to justify the exclusion of dermal and inhalation exposure. The document notes that numerous studies have found TBBPA

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[25] *See id.* at 70 (noting "effects on male reproductive organs" from a study in rats).

[26] *See id.* at 22.

[27] EPA, TSCA Work Plan Chemical Problem Formulation and Initial Assessment: Tetrabromobisphenol A and Related Chemicals Cluster Flame Retardants at 37 fig. 2-2.

in indoor air,[28] demonstrating a possibility of inhalation exposure . Yet the complete exclusion of these pathways of exposure/toxicity from the conceptual model suggestthese exposure pathways do not occur. This is inappropriate and deceptive in the face of exposure scenarios in the population. In the HBCD and CPE conceptual models, inhalation and dermal exposure pathways are at least depicted, even though OPPT decided not to quantify exposures from these pathways. These pathways must be included in the conceptual model for TBBPA.

The proposal to consider exposure to workers at manufacturing facilities and communities living nearby is appropriate, and it is also appropriate that bioconcentration into fish near manufacturing plants will be estimated. However, OPPT's argument against using a BCF 1200-1300 in fish[29] doesn't make sense. Total radioactivity, representing the parent compound and metabolites, reflects uptake of the parent compound. Considering only the parent compound underestimates the BCF.

OPPT proposes to ignore exposures to communities living near processing plants because TBBPA air emissions from processing plants are lower than emissions from manufacturing plants.[30] Although total air emissions may be lower at processing plant compared to a manufacturing plant, the routes and patterns of exposure may vary at the two, and the resulting exposures to nearby communities and ecosystems may therefore vary. These variations should be considered and calculated prior to determining that one scenario would be protective of the other. Furthermore, the background exposures for communities at each location (manufacturing and processing plants) may be different, and OPPT needs to account for this.

OPPT excludes water exposures (from drinking water generally, and for communities near wastewater treatment plants) from the exposure assessment because preliminary calculations show that the risk is low for the carcinogenic endpoint.[31] The logic here is faulty because: (1) the non-cancer endpoint is not considered and may be more sensitive and, more importantly, (2) even if the risk from the individual pathway is low, it will still contribute to aggregate risk. This exposure pathway must be retained in the assessment and added to the aggregate risk calculation.

As noted in our comments above, we disagree with OPPT's dismissal of studies demonstrating that microorganisms previously exposed to TBBPA degrade the compound.[32] In the environment, it is in fact likely that TBBPA degradation will take place by organisms in contaminated sites, so the available data are entirely appropriate to calculate the rate of TBBPA degradation to BPA and should be used to do so.

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[28] *See id.* at 31.
[29] *See id.* at 91.
[30] *See id.* at 35 tbl.2-6.
[31] *See id.* at 45-46.
[32] *See id.* at 92.

Comments on the hazard assessment

Consideration of both cancer and non-cancer endpoints is appropriate. The use of a linear dose-response relationship for cancer is appropriate given the lack of mechanistic data, and we recommend that OPPT follow the advice of the *Science and Decisions* report and use a unified dose-response framework for cancer and non-cancer endpoints (*see* Reference 17, Ch. 5).

Section 2.5.2 (human health hazards) of the TBBPA Problem Formulation and Initial Assessment seems to conclude that is the evidence of TBBPA's non-cancer effects is somehow equivocal. But, as OPPT notes earlier in the document, the California Safer Consumer Products Candidate Chemical list identifies the following hazard traits for TBBPA and TBBPA-bis(dibromopropyl ether) based on authoritative lists: endocrine toxicity, neurotoxicity, and reproductive toxicity.[33] OPPT implies that because the effects in the Nakajima et al. study did not show a classic dose-response the study should be discounted.[34] However, non-monotonic dose-effect functions are common in toxicity studies, especially when endocrine pathways are involved (*see* References 40–42). For motor tests, it is not uncommon for low and high doses to have different effects. For example, amphetamine increases activity at low doses and decreases it at high doses, going back through zero at some dose. The data on levels of TBBPA in the brain suggest specific effects at lower doses and non-specific effects at the highest dose.

Regarding the Saegusa et al. study (and OPPT's claim that "[i]t is not clear…whether offspring had direct access to TBBPA")it is well known that PND 0-10 in the rat represents the third trimester of pregnancy in humans with regard to brain development. Therefore the dosing regimen is optimally relevant.[35] Whether the pups had access to the chow is not problematic for interpretation of the study (and it is unlikely that they were eating chow at 0-12 days of age).

Regarding the Lilienthal et al. study[36]), although the use of albino animals is not optimal, it does not negate the possibility of auditory effects. The auditory function will be different from that of a pigmented rat, but any observed effects of a chemical represents impairment of nervous system function. As noted in our comments above, when a study is underpowered (i.e., using less than 10 animals per group) and still detects a statistically significant effect, that suggests that the effect is large. The effect should not be discounted because the study was underpowered.

OPPT asserts that there is "uncertainty in choosing a developmental toxicity study for evaluation in a quantitative risk assessment"[37] because there are a number of different effects seen in the studies. But it is to be expected that different endpoints will (or will not) be affected at different doses. OPPT states that the Fukuda study is the most appropriate to assess

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[33] *See id.* at 14.
[34] *See id.* at 32.
[35] *See id.* at 115.
[36] *See id.* at 113.
[37] *Id.* at 123.

developmental effects because of the dosing protocol.[38] This is not appropriate. As we note in our comments above, OPPT should rely on a well-conducted study (or studies) that finds the most sensitive effect (identifies effects at the lowest dose).

It appears that change in thyroid hormone levels is a consistent finding across a number of studies. This has large health implications since thyroid hormones are critical to a number of processes, including brain development, lipid metabolism, and cardiovascular function. For example, decreased thyroid hormone in pregnant women results in lower IQ in the offspring, even in women who are not considered to have clinically low thyroid levels. Miller et al.) and Woodruff et al. discuss how to interpret changes in thyroid hormones and perturbations in other organ systems in a risk assessment context (*see* References 16,43). Although changes on the individual level may seem insignificant, these changes interpreted to the population scale can be quite significant. Because individuals within a population express a range of thyroid hormone levels, an agent that causes a shift in the population will result in more individuals having clinically insufficient thyroid hormone levels. Therefore, the fact that changes in the levels seen in an animal toxicity study are not necessarily outside of "normal" range does not make the findings toxicologically insignificant (*see* Reference 44). TBBPA effects on thyroid should be included in the assessment and any change in thyroid homeostasis should be interpreted as an adverse effect.

Comments on the HBCD cluster

Based on the IRIS Toxicological Review of HBCD, the discussion of the literature in OPPT's Problem Formulation and Initial Assessment for Cyclic Aliphatic Bromides Cluster Flame Retardants is incomplete and inadequate. The IRIS review is also a year and a half out of date, so presumably even more studies are currently available. The IRIS document reviews epidemiological studies which are not cited in OPPT's problem formulation. The comments below on the individual studies are made in the absence of any such well laid out criteria, and should be integrated into the protocol we recommend developing for each chemical assessment.

The Problem Formulation and Initial Assessment notes at that the three chemicals identified for inclusion in the cluster have similar physical, chemical and environmental fate properties.[39] However, tetrabromocyclooctane (TBCO) is then excluded from cluster because uses were not identified. This raises a serious concern for this chemical's role as a potential regrettable substitute. TBCO is manufactured by Albemarle and identified as Saytex BCL-48 or Saytex BC-48 (*see* Reference 45), which searches identify as having a number of potential uses in polystyrene foams and textile coatings, similar to HBCD. TBCO should be included in the cluster for hazard analysis, even if exposure and risk cannot be calculated at this time. Qualitative conclusions can

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[38] *See id.* at 122.

[39] EPA, TSCA Work Plan Chemical Problem Formulation and Initial Assessment, Cyclic Aliphatic Bromides Cluster Flame Retardants, at 8.

still be drawn about the potential risks that could be posed if TBCO were used as an HBCD replacement.

Comments on the exposure assessment
The consideration of incidental ingestion by industrial workers and the recognition of exposure in microenvironments for toddlers are both appropriate.

It is unclear whether non-industrial workers (i.e., construction workers who handle, cut and install HBCD-containing products) will be assessed—exposures to these workers are noted in the document,[40] and these workers should be included in the assessment.

Inhalation of neat HBCD needs to be included in the aggregate exposure assessment for both workers and consumers. Even if these exposures "contribute less to overall exposure than the ingestion pathway,"[41] inhalation of neat HBCD still contributes to the total aggregate exposure and must be assessed.

Given OPPT's recognition of the very high BCF of HBCD in fish ,[42] it is critical to use data for subsistence fishers when assessing risks to indigenous populations that rely on fish and marine mammals, as well as other subsistence fisher populations. The 90th percentile from NHANES does not adequately capture high-end consumption.

Comments on the hazard assessment
It is unclear why OPPT concludes that "[t]oo little information is available in this study to determine the significance of its findings" regarding the Lilienthal et al. (2009) study.[43] The methods are clear and appropriate, and statistically significant changes were observed in auditory function in males at low frequencies. Because sexually-dimorphic response to toxic exposure is common in rodents, guideline protocols require testing both sexes. Otherwise testing one sex would be sufficient. It is also not uncommon to find differential effects at low and high frequencies resulting from exposure to chemicals or drugs. This finding represents a significant effect on nervous system function, and therefore represents an adverse effect.

In the Ema et al. study, dose-dependent changes were observed on tests of motor integration in females, but OPPT seeks to dismiss this result by claiming "[the] findings were not consistent" across sexes.[44] Again, sexually-dimorphic responses are common in rodent toxicity studies and that fact alone does not make the result questionable. OPPT should consider these results even if results are sexually-dimorphic.

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[40] *See id.* at 25, 35.
[41] *Id.* at 29.
[42] *See id.* at 22.
[43] *Id.* at 91.
[44] *Id.* at 91-92.

OPPT comments that the Eriksson et al. study finding effects on motor function in mice is not a GLP study and therefore they "reserve[] judgment."[45] As we discuss extensively in our comments above, the fact that a study was not conducted under GLP does not disqualify it. If GLP were an inclusion criterion, most of the literature would be excluded, leaving only industry studies for EPA to consider. Eriksson observed clear dose-response relationships on several measures and OPPT must use this finding in its assessment.

It is unclear what OPPT means in asserting that "[n]o standard neurotoxicity or developmental neurotoxicity studies ... are available."[46] As noted in the comments above, systematic criteria must be used in evaluating and selecting studies for inclusion, based on validity and relevance to the study question, without using the inappropriate assumption that only guideline protocol studies should be included.

CONCLUSION

The known toxicity and widespread presence of these flame retardant chemicals in everyday products and in almost every person elevates the importance of these assessments. We respectfully ask that OPPT release draft risk assessments for each flame retardant cluster and take public comment before finalizing the risk assessments.

Thank you for the opportunity to present these comments. We would be happy to discuss them with you at your convenience. We look forward to working with EPA to ensure that the risks associated with these flame retardant chemicals are accurately assessed, and that people and the environment are protected from adverse effects.

Sincerely,

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[45] *Id.* at 92.
[46] *Id.* at 90.

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Exhibit 1

Inhalation Exposure to Chlorinated Organophosphate and Other Flame Retardants: Respirable vs. Inhalable Intake

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WASHINGTON TOXICS COALITION

VIMS | William & Mary — VIRGINIA INSTITUTE OF MARINE SCIENCE

Background

The primary exposure route to most flame retardants (FRs) is believed to be ingestion of indoor dust, with inhalation as a contributing exposure [1, 2]. Allen et al., for example, examined inhalation exposure to the FRs polybrominated diphenyl ethers (PBDEs) and estimated inhalation exposure at a maximum of 22% of total [3].

Chlorinated organophosphate FRs (ClOPFRs) have been in heavy use in the U.S. for more than a decade but have not been widely studied in indoor air. Commonly used ClOPFRs include tris(1,3-dichloro-2-propyl)phosphate (TDCPP), tris(1-chloro-2-propyl)phosphate (TCPP), and tris(2-chloroethyl)phosphate (TCEP). TDCPP and TCEP have been designated as carcinogens, and all three have been banned from toys in the European Union.

Methods

Personal air of ten adults was tested using active air samplers; previous research found higher FR concentrations in personal air than in room air[3]. Two fractions were collected: respirable (< 4 µm, nominal) and inhalable (> 4 µm, nominal). Respirable dust penetrates deep into the lungs where gas exchange takes place. Larger particles are more likely to deposit in the airways of the head or the tracheobronchial region; they may then enter the body directly or be expelled via cilia and then swallowed, entering the digestive tract. Using simulated digestive fluid, Fang et al. estimated the bioaccessibility of ClOPFRs in dust at 80%[4].
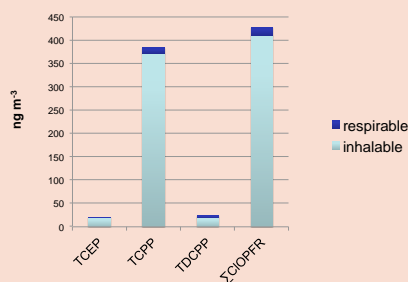
Air particulates were collected using an AirChek 2000 pump with an IOM Sampler with a stainless steel cassette [5]. Participants were instructed to wear the IOM sampler affixed to a collar for a 24-hour day during normal activities and to wear or hang it at breathing zone level during sleep. Inhalable particulates were collected with a MultiDust® foam disc of a specific porosity (D_{50}) of 4 µm; respirable particulates were collected on a 25-mm, 1.0 µm glass fiber filter placed in series behind the foam disc in the stainless steel cassette.

Air particulate samples (disc and filter) were analyzed for 22 FRs, including three ClOPFRs (TCEP, TCPP, and TDCPP) and 19 BFRs: PBDEs, TBB, TBPH, DBDPE, BDBPE, HBCDs, and TBBPA. FRs were analyzed by ultra-performance liquid chromatography (UPLC) - atmospheric pressure photoionization (APPI) tandem mass spectrometry[6].
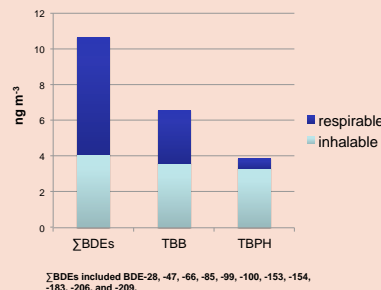
Estimates of intake from inhalation were created using median values from this study and an estimated adult inhalation rate of 13.25 m³ day⁻¹ [3]. These values were compared to estimates of intake from dust ingestion based on median values from previously collected dust from Washington state homes, a mean dust ingestion value of 4.16 mg day⁻¹, and a high value of 100 mg day⁻¹ [3,7].
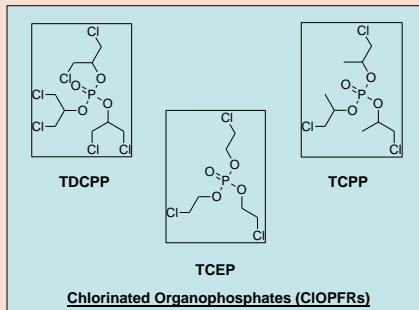
Figures

Figure 1: ClOPFR Concentrations, Air Particulates

Bar chart showing ng m⁻³ (0–450) for TCEP, TCPP, TDCPP, ∑ClOPFR with respirable and inhalable fractions.

Figure 2: BFR Concentrations, Air Particulates

Bar chart showing ng m⁻³ (0–12) for ∑BDEs, TBB, TBPH with respirable and inhalable fractions.

∑BDEs included BDE-28, -47, -66, -85, -99, -100, -153, -154, -183, -206, and -209.

Chemical structures: TDCPP, TCPP, TCEP — Chlorinated Organophosphates (ClOPFRs)

Results

ClOPFRs were detected in each set of air samples (respirable and inhalable) and were found at the highest concentrations. ∑ClOPFR levels ranged from 95.5 to 1190 m⁻³. TCPP was detected in the largest percentage of samples and at the highest levels. Levels and rates of detection were lower in the respirable fraction; the mean inhalable ∑ClOPFR air level was 408 ng m⁻³, compared to a mean respirable level of 15.3 ng m⁻³, indicating greater inhalation of the compounds associated with larger air particulates (Figure 1). These larger particulates may be trapped on the mucosa of the nose, mouth and lungs, preventing uptake from inside the lung but may still enter the vascular system through the digestive tract if swallowed. ClOPFRs were detected in seven of the nine respirable samples, however, and these particulates (< 4µm) can penetrate deep inside the lungs, allowing direct uptake of TCPP and TDCPP within the lung's gas-exchange region. These results show that ClOPFRs are airborne, capable of entering the airways through inhalation and transfer to the vascular system from the lungs and digestive tract. Recent research indicates that ClOPFRs have higher bioaccessibility following ingestion than other FRs, estimated at 80% compared to 25-60% for tested BFRs[4].

These levels compare with much lower detections of BFRs in this and previous studies in homes, although they are found at similar levels in house dust (Figure 2). In this study, ∑BDEs were detected at a mean level of 10.2 ng m⁻³.

Estimates of total intake from inhalation (Table 1) indicate that for ClOPFRs, the inhalation exposure route may be of particular importance. Estimated TCPP inhalation exposure approaches the California Prop 65 No Significant Risk Level of 5.4 µg day⁻¹ established for TDCPP. TCPP was found to have the highest house dust concentrations in a study of 20 Washington state homes and was detected at the highest concentrations in personal air sampling of four Washington state homes[6,7].

Table 1: Estimated Inhalation Exposure and Comparison to Dust Exposure

Compound	Air Estimated Intake ng day⁻¹	Dust Estimated Intake (mean) ng day⁻¹	Dust Estimated Intake (high) ng day⁻¹
∑BDEs	150	16.1	386
TBB	1.33	0.79	19.0
TBPH	1.99	0.48	11.5
TCEP	154	5.74	138
TCPP	3760	20.1	482
TDCPP	84.7	6.74	162

Air intake estimates based on inhalation rate of 13.25 m³ day⁻¹. Mean dust intake estimates based on ingestion rate of 4.16 mg day⁻¹; high dust intake estimates based on 100 mg day⁻¹[3].

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Exhibit 2

INHALATION EXPOSURE TO CHLORINATED ORGANOPHOSPHATE FLAME RETARDANTS: RESPIRABLE VS. INHALABLE INTAKE

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Introduction

Chlorinated organophosphate flame retardants (ClOPFRs) have been in heavy use in the United States for more than a decade. In the last five years, product testing has revealed the frequent presence of two compounds, tris(1,3-dichloro-2-propyl)phosphate (TDCPP), and tris(1-chloro-2-propyl)phosphate (TCPP), in polyurethane foam in residential furniture and children's products[1-3]. Another compound, tris(2-chloroethyl)phosphate (TCEP), has also been detected in these products. Both TDCPP and TCEP have been designated as carcinogens by government agencies, and the European Union has classified TCEP as a CMR substance. All three compounds have been banned from toys in the European Union under its toy safety directive beginning December 31, 2015[4]. TCPP has received less study, but its use appears to be on the rise as manufacturers phase out production of TDCPP, and U.S. production and import were most recently reported at nearly 25,000 tons[5].

For the general public, the primary exposure route to most flame retardants is believed to be incidental ingestion of contaminated indoor dust, with inhalation as a contributing exposure [6, 7] Allen et al. examined potential inhalation using personal samplers worn by study participants[8]. They estimated inhalation exposure at up to 22% of total for BDE-209, and concluded inhalation may be more important than previously hypothesized due to the presence of a cloud of suspended particles generated by participant activities. At room temperature flame retardants such as PBDEs have a high affinity for air particulates and exhibit low concentrations in the vapor state. These dust particulates may then penetrate deep inside the lung when inhaled.

Inhalation exposure may be a more important exposure route for ClOPFRs than it is for brominated flame retardants such as PBDEs. However, previous indoor air testing for ClOPFRs has been limited, particularly in the US. The present study tested the personal air of nine adults using active air samplers; previous research has found higher flame retardant concentrations in personal air than in room air[8]. To determine the extent to which these compounds penetrate deep into the lungs, two fractions were collected: respirable (less than 4 µm, nominal) and inhalable (less than 100 µm, nominal). Inhalable dust can be deposited anywhere in the respiratory tract, whereas respirable dust penetrates deep into the lungs where gas exchange takes place. The larger particles are more likely to deposit in the airways of the head or the tracheobronchial region; they may then enter the body diretly or be expelled via cilia and mucus into the mouth and then swallowed and enter via the digestive tract.

Materials and Methods

Air sampling method:

Air particulates were collected using an AirChek 2000 pump (flow rate 2 L min^{-1}) with an Institute of Occupational Medicine (IOM) Sampler equipped with a stainless steel cassette assembly [9]. Participants were instructed to wear the IOM sampler affixed to a collar continually during a 24-hour day during normal activities, including at home and at work, traveling to and from home and work, shopping, and socializing, and to wear or hang the sampler at breathing zone level during sleep. Time of collection ranged from 12.9 to 24.6 hours. The IOM sampler meets air particulate sampling criteria established by the American Conference of Governmental Industrial Hygienists (ACGIH) and the Occupational Safety and Health Administration (OSHA)[9].Two size classes of air particulates were examined: 1) inhalable particulates (> 4 µm, nominal), that can either enter the lung airways (trachea, bronchi and their branches) or are trapped on the mucosa of the nose, mouth and lungs and then are expelled or swallowed. These were collected with

a MultiDust® foam disc of a specific porosity (D_{50}) of 4 µm (D_{50}: a particle aerodynamic diameter for which 50% of the particles penetrate). This was placed inside the stainless steel cassette assembly, positioned at the IOM inlet; 2) smaller respirable air particulates (< 4 µm, nominal) which are able to penetrate deep inside the lung's gas-exchange regions were collected on a 25-mm, 1.0 µm glass fiber filter placed in series behind the foam disc within the cassette. After collection, all sample cassettes were placed in SKC's transportation clip with cover and stored <4°C in double sealed plastic bags until analyzed.

Analytical protocol (Extraction, purification and analysis):

Air particulate samples (disc and filter) were analyzed for ClOPFRs (i.e. TCEP, TCPP and TDCPP) as described by La Guardia et al.[10]. Briefly, samples were spiked with a surrogate standard (deuterated tris (1,3-dichloro-2-propyl)phosphate (*d*TDCPP), Max Planck Institute for Biophysical Chemistry, Germany) and extracted with methylene chloride (DCM) in a Dionex ASE 200 accelerated solvent extractor (Sunnyvale, CA, USA) at 100°C and 68 atm. Each extract was then purified on a 2 gm silica solid phase extraction column (International Sorbent Tech.; Hengoed Mid Glamorgan, UK) eluted with 3.5-mL hexane (Fraction 1), followed by 6.5 mL of 60:40 hexane/DCM and then 8 mL DCM (Fraction 2) and 5 mL 50:50 acetone/DCM (Fraction 3). Fraction 3 containing the analytes of interest was reduced; solvent exchanged to methanol and decachlorodiphenyl ether (DCDE, AccuStandards, Inc.) was added as the internal standard. Analytes within each purified extract were further separated by ultra-performance liquid chromatography (UPLC, Waters Corp. Milford, MA, USA) and analyzed by atmospheric pressure photoionization tandem mass spectrometry (APPI/MS/MS, Q-Trap3200 MS, AB Sciex, Framingham, MA. USA).

Results and Discussion

ClOPFRs were detected in each set of air samples (respirable and inhalable), indicating that inhalation can be an important route of exposure. ∑ClOPFR levels ranged from 95.5 to 1190 ng m^{-3} (Table 1). TCPP was detected in the largest percentage of samples and at the highest levels. It was detected in all of the inhalable air samples (mean 371, range 16.0 to 1180 ng m^{-3}), contributing > 61% to their total in all but one sample (#6I) which was dominated by TDCPP, contributing 74% to its total. Levels and rates of detection were lower in the respirable fraction; means were 11.1 ng m^{-3} (range 8.17 to 28.6) for TCPP, detected in five of nine samples, and 4.79 ng m^{-3} (range 3.25 to 20.9) for TDCPP, detected in four of nine samples; TCEP was not detected. The mean inhalable ∑ClOPFR air level was 408 ng m^{-3}, compared to a mean respirable level of 15.3 ng m^{-3}, indicating greater inhalation of the compounds associated with larger air particulates (Figure 1). These larger particulates may be trapped on the mucosa of the nose, mouth and lungs, preventing uptake from inside the lung but may still enter the vascular system through the digestive tract if swallowed. ClOPFRs were detected in seven of the nine respirable samples, however, and these particulates (< 4um) can penetrate deep inside the lung region, allowing direct uptake of TCPP and TDCPP within the lung's gas-exchange region. These results show that ClOPFRs are airborne, capable of entering the airways through inhalation and transfer to the vascular system from the lungs and digestive tract.
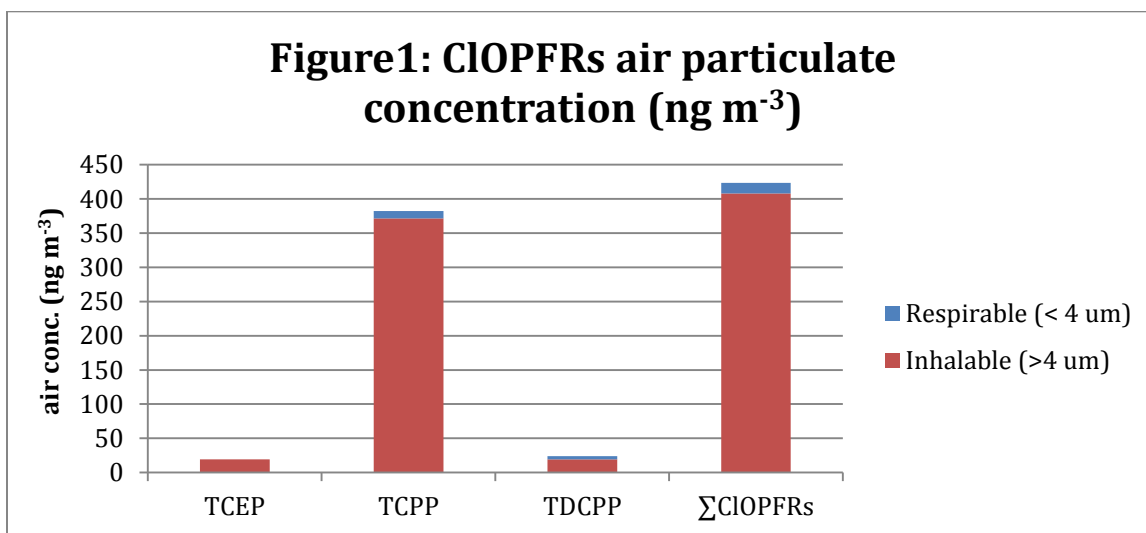
Table 1: ClOPFRs respirable and inhalable air particulate concentrations.

Respirable (< 4 µm), ng m^{-3}		3R	5R	6R	7R	8R	9R	10R	11R	12R	min	max	Mean[1] (n=9)
	TCEP	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd	nd
	TCPP	nd	22.3	13.5	28.6	24.4	8.17	nd	nd	nd	nd	28.6	11.1
	TDCPP	3.25	nd	20.9	5.43	nd	9.86	nd	nd	nd	nd	20.9	4.79
	∑ClOPFRs	3.25	22.3	34.4	34.0	24.4	8.17	9.86	nd	nd	nd	34.4	15.3

Inhalable (> 4 µm), ng m^{-3}		3I	5I	6I	7I	8I	9I	10I	11I	12I	min	max	Mean[1] (n=9)
	TCEP	77.8	17.5	nd	14.0	9.41	3.36	11.1	27.4	10.6	nd	77.8	19.1
	TCPP	248	262	16.0	255	509	1180	312	134	424	16.0	1180	371
	TDCPP	82.2	40.0	45.2	nd	nd	nd	nd	nd	nd	nd	82.2	19.1
	∑ClOPFRs	408	320	61.1	269	518	1180	323	162	434	61.1	1180	408

| Total (respirable + Inhalable) ClOPFRs | 411 | 342 | 95.5 | 303 | 542 | 1190 | 333 | 162 | 434 | 95.5 | 1190 | 424 |

These levels compare with much lower detections of PBDEs in previous studies in homes, although they are found at similar levels in house dust. Allen et al., for example, found a geometric mean level of 0.77 ng m^{-3} ∑PBDEs in 20 Boston homes sampled in 2006[8]. Mean levels of ∑PBDEs in an electronics recycling facility in Sweden were measured at 6.2 ng m^{-3} in room air samples collected in 2002[11]. Hartmann et al. conducted area sampling for TCEP, TCPP, and other compounds in Switzerland in a variety of locations, including cars, furniture stores, offices, and electronics stores[12]. In that study, TCPP was also present at the highest levels, ranging up to 260 ng m$^{-3.}$ Mäkinen et al. used personal air samplers to investigate occupational exposure to ClOPFRs in Finland, and both TCEP and TCPP were frequently detected, with levels up to 1,100 ng m^{-3}[13]. Finally, Marklund et al. conducted area sampling in a number of domestic and occupational environments in Sweden, with detections up to 590 ng m^{-3}[14].

These results indicate that for ClOPFRs in particular, the inhalation exposure route may be of particular importance. They also add to growing evidence of exposure to TCPP, recently found to have the highest house dust concentrations in a study of 20 Washington state homes[15]. TCPP was also detected at the highest concentrations in personal air sampling of four Washington state homes[10]. The compound has not been highly regulated, but is the subject of concern because of its molecular similarity to TCEP and TDCPP, two compounds with known toxicity. TCPP was included in a proposed flame retardant ban introduced to the US Senate in 2014[16].

Figure1: ClOPFRs air particulate concentration (ng m^{-3})

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