United States
Environmental Protection Agency

Office of Chemical Safety and
Pollution Prevention
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Summary of External Peer Review and Public Comments and Disposition for Cyclic Aliphatic Bromide Cluster (HBCD)

Response to Support Risk Evaluation of Cyclic Aliphatic Bromide Cluster (HBCD)

September 2020

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EPA published the Draft Risk Evaluation for Cyclic Aliphatic Bromide Cluster (HBCD) in June 2019 and accepted public comments until August 28, 2019. Materials on the draft risk evaluation are available in docket EPA-HQ-OPPT-2019-0237. EPA held a peer review meeting of EPA's Science Advisory Committee on Chemicals (SACC) on the draft risk evaluation for this chemical's condition of use on July 30-31, 2019.

This document summarizes the public and external peer review comments that the EPA's Office of Pollution Prevention and Toxics (OPPT) received for the risk evaluation of Cyclic Aliphatic Bromide Cluster (HBCD). It also provides EPA's response to the comments received from the public and the peer review panel.

EPA appreciates the valuable input provided by the public and peer review panel. The input resulted in numerous revisions to the risk evaluation document.

Peer review charge questions[1] are used to categorize the peer review and public comments into specific issues related to the five main themes.

1. Content, Organization and Clarity of the Document
2. Clarity in the Description of Literature Search, Literature Screening, and Data Evaluation
3. Environmental Exposure Assessment, Including Environmental Fate and Transport and Environmental Release Assessment
4. Hazard and Dose Response Assessment, Including Ecological, Occupational, General Population, and Consumer Receptors
5. Risk Characterization

All peer review comments for the eight charge questions are presented first, organized by charge question. These are followed by the public comments. For each theme, general comments pertaining to all chemicals are presented first, and then additional comments pertaining to only one or several chemicals follow.

[1] These are the questions that EPA submitted to the panel to guide the peer review process.

ABBREVIATIONS

7Q10	Lowest expected weekly flow over a ten-year period
ADME	Absorption, Distribution, Metabolism, and Excretion
APF	Assigned Protection Factors
ATSDR	Agency for Toxic Substances and Disease Registry
BAF	Bioaccumulation Factor
BCF	Bioconcentration Factor
BMD	Benchmark Dose Modeling
BMDL	Lower Confidence limit on the BMD
BMR	Benchmark Response
CDR	Chemical Data Reporting
CHAD	Consolidated Human Activity Database
COC	Concentration of Concern
COU	Condition of Use
ECHA	European Chemicals Agency
ECOTOX	ECOTOXicology knowledgebase
E-FAST	Exposure and Fate Assessment Screening Tool
EPS	Expanded Polystyrene
ER	Extra Risk
ESD	Emission Scenario Document
EU	European Union
EURAR	European Union Risk Assessment Report
FR	Federal Register
GI tract	Gastrointestinal tract
g	Gram
HBCD/HBCDD	Hexabromocyclododecane
HERO	Health and Environmental Research Online
HIPS	High Impact Polystyrene
HPLC	High Performance Liquid Chromatography
HQ	Headquarters
hr	Hour
IECCU	Indoor Environmental Concentrations in Buildings with Conditioned and Unconditioned Zones
IIOAC	Integrated Indoor-Outdoor Air Calculator
KABAM	K_{OW} (based) Aquatic BioAccumulation Model
kg	Kilogram(s)
Koa	Octanol:Air Partition Coefficient
L	Liter(s)
lb	Pound
LOAEL	Lowest Observed Adverse Effect Level
LOEC	Lowest Observed Effect Concentration
Log Koc	Logarithmic Organic Carbon:Water Partition Coefficient

Log Kow	Logarithmic Octanol:Water Partition Coefficient
m^3	Cubic Meter(s)
MOA	Mode of Action
MOE	Margin of Exposure
MOEJ	Ministry of Environment Government in Japan
MSW	Municipal Solid Waste
MSWLF	Municipal Solid Waste Landfills
ND	No Data
NICNAS	National Industrial Chemicals Notification and Assessment Scheme
NIOSH	National Institute for Occupational Safety and Health
NOAEL	No Observable Adverse Effect Level
NOEC	No Observed Effect Concentration
OES	Occupational Exposure Scenario
ONU	Occupational Non-User
OPPT	Office of Pollution Prevention and Toxics
OSHA	Occupational Safety and Health Administration
PBDE	Polybrominated Diphenyl Ether
PBPK	Physiologically Based Pharmacokinetic Model
PDM	Probabilistic Dilution Model
PESS	Potentially Exposed or Susceptible Subpopulations
PNOR	Particles Not Otherwise Regulated
POD	Point of Departure
POPs	Stockholm Convention on Persistent Organic Pollutants
POTW	Publicly Owned Treatment Works
ppm	Part(s) per Million
RAR	Risk Assessment Report
RCRA	Resource Conservation and Recovery Act
REACH	European Union's Registration, Evaluation, Authorisation and Restriction of Chemicals
SIPS	Structural Insulated Panels
SNUR	Significant New Use Rule
SOD	Superoxide dismutase
TGD	Technical Guidance Document
TRI	Toxics Release Inventory
TSCA	Toxic Substances Control Act
TSH	Thyroid Stimulating Hormone
TWA	Time-Weighted Average
UF	Uncertainty Factor
U.S.	United States
UNEP	United Nations Environment Programme
VVWM-PSC	Variable Volume Water Model - Point Source Calculator
WWT/WWTP	Wastewater Treatment Plant
XPS	Extruded Polystyrene (*i.e.*, Extruded Polystyrene foam)
XPSA	Extruded Polystyrene Association

List of Comments		
Comment #	**Docket File**	**Submitter**
24	EPA-HQ-OPPT-2019-0237-0024	Safer Chemicals Healthy Families
28	EPA-HQ-OPPT-2019-0237-0028	Environmental Protection Network
29	EPA-HQ-OPPT-2019-0237-0029	Earthjustice and Occupational Safety & Health Law Project LLC
30	EPA-HQ-OPPT-2019-0237-0030	Environmental Defense Fund
31	EPA-HQ-OPPT-2019-0237-0031	American Chemistry Council
33	EPA-HQ-OPPT-2019-0237-0033	Environmental Protection Network
41	EPA-HQ-OPPT-2019-0237-0041	State of Washington
43	EPA-HQ-OPPT-2019-0237-0043	MacRoy
44	EPA-HQ-OPPT-2019-0237-0044	Singla
45	EPA-HQ-OPPT-2019-0237-0045	Hartigan
47	EPA-HQ-OPPT-2019-0237-0047	Motor & Equipment Manufacturers Association
48	EPA-HQ-OPPT-2019-0237-0048	Environmental Protection Network
49	EPA-HQ-OPPT-2019-0237-0049	Alliance of Automobile Manufacturers
50	EPA-HQ-OPPT-2019-0237-0050	American Chemistry Council & NAFRA

51	EPA-HQ-OPPT-2019-0237-0051	American Chemistry Council
53	EPA-HQ-OPPT-2019-0237-0053	Alaska Community Action on Toxics
54	EPA-HQ-OPPT-2019-0237-0054	National Tribal Toxics Council
55	EPA-HQ-OPPT-2019-0237-0055	Occupational Safety & Health Law Project
56	EPA-HQ-OPPT-2019-0237-0056	Environmental Defense Fund
57	EPA-HQ-OPPT-2019-0237-0057	Safer Chemicals Healthy Families
58	EPA-HQ-OPPT-2019-0237-0058	Extruded Polystyrene Foam Association
59	EPA-HQ-OPPT-2019-0237-0059	UCSF
61	EPA-HQ-OPPT-2019-0237-0061	Environmental Risk Reduction and Project TENDR
62	EPA-HQ-OPPT-2019-0237-0062	Earthjustice
63	EPA-HQ-OPPT-2019-0237-0063	Toxics Use Reduction Institute

Content and Organization – Public and Peer Review Comments		
Charge Question 1.1: Please comment on the overall content, organization, and presentation of the draft risk evaluation for HBCD. **Charge Question 1.2: Please provide suggestions for improving the clarity of the information presented in the documents.**		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 1**	**EPA/OPPT Response**
Inconsistencies/errors		
SACC	**SACC COMMENTS:** • A committee member expressed some concern that there are discrepancies regarding exposure assessments of polystyrene (PS) insulation exposure, particularly on page 39 where text indicates reuse and/or disposal will not be evaluated. (p. 91)	EPA stated in the draft risk evaluation that "reuse, disposal, and recycling of HBCD-containing products from legacy uses are not within the conditions of use of the draft risk evaluation." This statement applied to use and disposal of articles such as electronics devices for which HBCD manufacture, processing, and distribution for such use had ceased, but not to use and disposal of polystyrene insulation. EPA evaluated exposure from use of EPS and XPS containing HBCD; recycling of EPS and reuse of XPS; and disposal of EPS and XPS in the final risk evaluation. For the final risk evaluation, EPA also assessed recycling of HBCD containing high impact polystyrene (HIPS) in electronics products. In addition, due to a 9th Circuit Court of Appeals ruling in *Safer Chemicals, Healthy Families v. EPA*, EPA considered formerly termed "legacy uses" and "associated disposal" as uses and disposal, respectively, within the definition of "conditions of use." In the final risk evaluation, EPA discusses these "legacy" uses of HBCD in products and articles, and disposal of those products and articles, in Section 1.2.8 of the final risk evaluation.
SACC	**SACC COMMENTS:** • Page 31 – Missing hyperlink to (EPA-HQ-OPPT-2016-0735-0049) in Section 1.2.1 (p. 93)	EPA has added hyperlink.

SACC	**SACC COMMENTS:** • Inconsistent use of past, present, and future tense. (See for example Section 4.1.1.1 where "are based," "is based," and "will be based" are used in the same paragraph. "are/is based" should be consistently used.) (p. 94)	EPA has revised use of tense throughout the document.
SACC	**SACC COMMENTS:** • In 3.1.1 (page 278) the document references the data quality evaluation results in the statement: "The data quality evaluation results are outlined in Tables 1 and 2 in Appendix G of this document…" The data quality result tables referenced here can be found in the supplemental document Risk Evaluation for Cyclic Aliphatic Bromide Cluster (HBCD), Systematic Review Supplemental File: Data Extraction Tables of Environmental Hazard Studies. (U.S. EPA 2019), which is indirectly referenced in Appendix G.1. (p. 93)	EPA corrected the reference to Table 2 Appendix D.
Add discussion of the role of micro- and nano-plastic		
SACC	**SACC COMMENTS:** • Mentioned in the uncertainty analyses is the fact that the fate and biological effects of HBCD compounds are stereoselective, and the fact that there is limited data on these diastereomers.[3] This should probably be mentioned in the Introduction. In addition, a limited discussion of the role of micro- and nano-plastic inputs from HBCD-containing polystyrene as vectors to aquatic systems could be included. (p. 92)	EPA has added text discussing the role of microplastics as HBCD vectors to aquatic systems in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport. Isomers specifically are named in section 1.1 Physical-Chemical properties.
SACC	**SACC COMMENTS:** • Consider including a limited discussion of the role of micro- and nano-plastic inputs from HBCD-containing polystyrene as vectors to aquatic systems. (p. 93)	EPA has added text discussing the role of microplastics as HBCD vectors to aquatic systems in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport.
Editorial/Clarification		
SACC	**SACC COMMENTS:** • The use of references to other relevant sections of the report, supporting information, and appendices, and hyperlinks between those references are helpful to the reader. Hyperlinks in the Table of Contents were also useful. In addition to hyperlinks**,** it was suggested that the Agency provide location information (*e.g.,* page number, chapter) where applicable when citing reference documents. (p. 91)	Section numbers are cited and hyperlinked, but not page numbers under current formatting guidance.

SACC	**SACC COMMENTS:**
	• Several Committee members suggested that adding a brief discussion on why the substance was initially selected for review would help to make the document more complete. Additionally, the Introduction could include:
	  • A summary of scoping and problem formulation findings
	  • The initial conceptual model as well as the final model on which the Evaluation is based
	  • Background information on HBCD's manufacturing and production to provide context for the assessment. (p. 91)
	• Include a brief discussion on why the chemical was originally included in the Work Plan. (p. 93)
	• Include a summary of scoping and problem formulation in the Introduction. (p. 93)
		To avoid confusion and ensure clarity in the evaluations presented in the final risk evaluation, the final risk evaluation does not include draft versions of conceptual models or any other analyses. Additionally, background information on HBCD manufacturing and import are provided in Section 1.2.2 and 1.2.1, respectively. A short summary of the scope and problem formulation is included in the Introduction of the risk evaluation. Further details are all provided in the original HBCD Scope and Problem Formulation documents, which are referenced and hyperlinked within the Risk Evaluation.

SACC	**SACC COMMENTS:** • There was some concern that the Evaluation, as currently drafted, seems to contain a lot of repeated text, and this repetition may be due to the way the document is structured. Using a structure like that used in the presentation might lead to reduction in repetition and hence to a shorter and more concise risk assessment document. (p. 91)	EPA is maintaining the current format for the Final Risk Evaluation in order to remain consistent with all other First 10 chemical evaluations. However, EPA acknowledges this comment and will consider changes to the document format for future evaluations.
SACC	**SACC COMMENTS:** • It was also noted that the graphics and tables used in the summary presentation may also be helpful in the document itself to improve clarity. (p. 91)	EPA has incorporated descriptive graphics based on the SACC presentation into the risk evaluation, where useful.
SACC	**SACC COMMENTS:** • In general, the Committee encourages the use of graphics, tables or bulleted lists. For instance, on pages 26 and 27 under Risk Determination, the sentence starting with "… EPA considered relevant risk-related factors, including, but not limited to: …" could be made into bullets, and the graphic from slide 19 of the summary presentation could be added to Section 2.2. (pp. 91-92)	The format of the executive summary has been updated to be consistent with other TSCA chemical Risk Evaluations.
SACC	**SACC COMMENTS:** • Increase use of graphics, tables, and bulleted lists where possible, to improve	EPA has incorporated descriptive graphics based on the SACC presentation into the risk evaluation, where useful.

	clarity. (p. 92)	
SACC	**SACC COMMENTS:** • The definition of "reasonably available" as a modifier of sources of information/data is inadequate. (*e.g.,* one definition stated "reasonably" available literature is that which can be "reasonably" obtained). Similarly, the Evaluation needs to define the terms "conditions of use" and "exposure scenarios" and how they are used. (p. 92)	TSCA section 26(k) directs EPA to take into consideration information related to a chemical substance that is "reasonably available" to the Agency when carrying out TSCA section 6(b) risk evaluations. The term "reasonably available information" is defined in EPA's risk evaluation rule (Procedures for Chemical Risk Evaluation Under Amended TSCA, 40 CFR 702.33): "*Reasonably available information* means information that EPA possesses or can reasonably generate, obtain, and synthesize for use in risk evaluations, considering the deadlines specified in TSCA section 6(b)(4)(G) for completing such evaluation." "Conditions of use" is defined in TSCA Section 3(4): "*Conditions of use* means the circumstances, as determined by the Administrator, under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." TSCA Section 6(b)(4) directs EPA to conduct risk evaluations to determine whether a chemical substance presents an unreasonable risk under the conditions of use. "Exposure scenarios" are a technical term within the risk evaluation used to refer to occupational situations that may result in differing exposures and releases relative to other scenarios. Multiple scenarios may fall within a single COU.
SACC	**SACC COMMENTS:** • The Evaluation would benefit from an Index. EPA could consider pulling out Data Integration as its own section. (p. 92)	The risk evaluation contains a Table of Contents with links to every section, table, and figure. WOE (weight of the scientific evidence) sections are intended to serve as a data integration

		section. Data integration is also considered in selection of studies for POD derivation.
SACC	**SACC COMMENTS:** • Consider mentioning in the Introduction the fact that the fate and biological effects of these compounds are stereoselective, and there is limited data for the diastereomers. (p. 93)	This information has been added to the description of Physical-Chemical Properties in Section 1.1.
SACC	**SACC COMMENTS:** • Page 24, 1st sentence – EPA has concluded that manufacturing by large manufacturers has ceased, at least in the U.S., based on communications with industry, and it is assumed that for small manufacturers, it would be cost prohibitive to produce HBCD in small quantities." (p. 93)	This change has been incorporated with minor edits for clarity.
SACC	**SACC COMMENTS:** • Page 29, 4th paragraph, last sentence – "Section 5 presents EPA's proposed determination of whether the chemical presents and unreasonable risk under the conditions of use, as required under TSCA 15 U.S.C. 2605(b)(4)." (p. 93)	This text has been removed as part of updates to the executive summary for the final risk evaluation.
SACC	**SACC COMMENTS:** • Page 30, 2nd paragraph – "As explained by the EPA in the Risk Evaluation Rule (82 Fed. Reg. 33726 (July 20, 2017)), it is important for peer reviewers to consider the logical presentation of the underlying risk evaluation analyses and the extent to which results support an integrated risk characterization on which the conclusion of an unreasonable or not-unreasonable risk determination is made." (p. 93)	This change has been incorporated.
SACC	**SACC COMMENTS:** • Page 50, Section 1.5, 2nd paragraph – Citation needed in last line- "considering the deadlines for completing the evaluation (Citation to Final Rule)." (p. 93)	The citation and hyperlink have been added.
SACC	**SACC COMMENTS:** • The Committee found Slides 7 – 11 of the EPA[5] (at-meeting) technical presentation from Dr. Wong particularly helpful in understanding the links between EPA's included uses, conditions of use, and how that leads to specific releases that expose the various considered receptors. The Committee	EPA has improved clarity in the explanation of COUs and exposure scenarios. Several diagrams have also been incorporated into the exposure section as recommended.

	recommended including these figures in the Evaluation document. (p. 100)	
SACC	**SACC COMMENTS:** • The Committee recommended including references in tables where appropriate and in addition, it would be helpful to include conclusions/summaries reached at the end of each section. (p. 101)	EPA has included additional table references and section summaries where appropriate.
#	**Summary of Public Comments for Specific Issues Related to Charge Question 1**	**EPA/OPPT Response**
General		
49 24, 57 51	**PUBLIC COMMENTS:** • An insufficient amount of time was allotted for public comment prior to the scheduled Science Advisory Committee on Chemicals (SACC) meeting. The deadline for written comments was Aug. 30th; however, the SACC meeting began on July 29th. As a result, the full set of comments were not provided to the SACC. This conflicts with the recommendation in the EPA Peer Review Handbook to accept public comments prior to peer review. What was the reasoning for this set schedule? • If the public wanted to submit comments in time for the SACC meeting, written submissions had to be made by July 19th, which allowed the public less than three weeks after EPA announced the availability of the drafts to review the material. This was not enough time to conduct an informed and comprehensive review. • The Populations, Exposures, Comparators and Outcomes (PECO) statements established during scoping should define the scope and focus of the systematic review and should be included in the Risk Evaluation. The pathways and Processes, Exposure, Setting or Scenario, and Outcomes (PESO) statement, which was used during the full text screening of environmental fate and transport data sources, and the Receptors, Exposure, Setting or Scenario, and Outcomes (RESO) statement, which was used during the full text screening of the engineering and occupational exposure literature, should be included directly in the risk evaluation document.	The Lautenberg amendments to TSCA provide a three- and one-half-year timeframe for completion of existing chemical risk evaluations. However, in the first year following enactment, EPA's focus was on issuing the Risk Evaluation Rule outlining the framework for implementing TSCA Section 6(b). Consequently, the time for completing the first 10 risk evaluations has been compressed. As discussed in the Introduction, EPA believed peer reviewers were most effective in this role if they received the benefit of public comments on draft risk evaluations prior to peer review. For this reason, and consistent with standard Agency practice, the public comment period preceded peer review. The final risk evaluation changed in response to public comments received on the draft risk evaluation and/or in response to peer review, which itself may be informed by public comments. EPA will consider these comments for future risk evaluations. PECO and PESO statements are included in appendix E of the Problem Formulation. The Problem Formulation is referenced in the Risk Evaluation with a hyperlink to the PDF.
Editorial/Clarification		

	PUBLIC COMMENTS:	A risk conclusions Section 4.5 has been added that links the risk characterization results to the risk determination. This section includes summary tables which display the values that will be considered for risk determination. EPA has reviewed all the risk determinations in the draft risk evaluation to correct any inconsistencies in the approach for determining unreasonable risk, including assumptions regarding the use of PPE in each condition of use. In response to comments on the first ten chemical risk evaluations, EPA revised the structure and content of the unreasonable risk determination sections including Table 5-1. In the final risk evaluation, Table 5-1 does include citations to the detailed risk determination sections. In addition, EPA has added risk conclusion sections in Section 4.5 to summarize risk for environmental and human health.
31	• The draft risk evaluation does not provide adequate citations. o The final risk determination sections should be clarified. EPA should cite the relevant supporting scientific information (section/page/table numbers from the draft risk evaluation) for each decision made under the risk determination section. o Where EPA reports the finding of no unreasonable risk when personal protective equipment (PPE) is used, a citation to the margin of exposure (MOE) found when using PPE should be included. o All evidentiary findings should be appropriately cited so that the public may more easily understand the conclusions drawn in the risk determination.	
51	• Table 5.1 is not organized in a way that is easily understandable. It should cite the sections in the risk characterization that provide the reader with the supporting evidence. o The "presents" and "does not present" statements should cite to the additional statutory and regulatory requirements that the determinations are based upon best available science, weight of the scientific evidence, and data quality. o EPA should consider including a modified table that represents the relevant endpoints and drivers, potentially color-coded with regard to those that exceed benchmarks.	
45	• The risk determination section does not clearly link the exposure scenarios to the ultimate risk determinations. Section 5 requires more attention if it is going to serve as a solid risk communication tool to the public. o This section should clearly explain how the environmental assessments that were performed informed the risk determinations. o EPA should clarify the basis for the determinations in order to improve the public's understanding of them. o For example, for several conditions of use, the risk determination section includes a description of the environmental exposure scenario with the highest risk estimate, the environment risk driver benchmark of > 1, and the environment risk estimate based on monitoring data which exceed this benchmark. ▪ Yet the risk determination for the environment was "no unreasonable risk."	

	▪ This needs further clarification because it does not include an adequate explanation of how EPA used this information to arrive at this determination. ▪ To the extent that EPA used some of the additional sensitivity analyses and other relevant information to inform this decision, this should be more adequately described.	
61	**PUBLIC COMMENTS:** • The risk evaluation should clarify whether the exposure assessment fully considered children's exposure.	EPA evaluated children's mouthing of products containing HBCD in the draft risk evaluation and has added additional context and transparency to this evaluation in the final risk evaluation (Sections 2.4.4.4 and 4.2.3.3.1). Risk estimates for the most sensitive life stage were almost a full order of magnitude above the benchmark MOE (indicating very low risk). This risk estimation is independent of production volume and was based on reasonably available information on exposure and toxicity to HBCD in these products. Children's exposures were also evaluated based on conditions of use and general population (background) using modeled and monitoring data, respectively.
44	**PUBLIC COMMENTS:** • Data tables in the draft risk evaluation and supplementary files provided do not identify what the key sources are.	Many tables contained source descriptions in footnotes or the preceding description. Key source citations have been added for tables which were not previously cited.
30, 56	**PUBLIC COMMENTS:** • EPA's description of its intended approach to dose-response modeling lacks sufficient explanation, details and scientific justification: Section 17 (p. 78).	EPA used benchmark dose modeling for all endpoints which offers more precision than a NOAEL or LOAEL approach. A detailed description of benchmark dose modeling, including model selection, is provided in Section 3.2.5.2 and methodologies used are from established EPA guidance (U.S. EPA 2012a).
62	**PUBLIC COMMENTS:** • Regarding the drinking water pathway, EPA claims that "a qualitative	EPA has removed the statement referencing Section 2.4.2.7 from the final Risk Evaluation.

	discussion of this [pathway] is included in Section 2.4.2.7," however, this section does not mention drinking water.	As stated in the Introduction, further analysis subsequent to the HBCD Problem Formulation was not conducted for the drinking water pathway based on a qualitative assessment of the physical chemical properties and fate of HBCD in the environment.
44	**PUBLIC COMMENTS:** • There is discordance between ratings reported in the draft risk evaluation and in the supplementary scoring sheets – for example, on p. 184 of the draft risk evaluation, the source "ECHA (2009c)" for inhalation of HBCD during packaging is listed with an overall confidence rating of "high," while on p. 240 of the Systematic Review Supplemental File: Data Quality Evaluation of Environmental Releases and Occupational Exposure Data, this source is listed as unacceptable.	EPA has corrected the rating to in the final risk evaluation to be the same as the Systematic Review Supplemental File: Data Quality Evaluation of Environmental Releases and Occupational Exposure Data.
59	**PUBLIC COMMENTS:** • In the risk evaluation it states that EPA "assume[s] workers are properly trained and fitted on respirator use, and that they wear respirators for the entire duration of the work activity … throughout their career" but it later states "regular use of respirators in chronic scenarios may not always be feasible." o EPA must reconcile these inconsistent statements.	While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether or not a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. In response to SACC feedback and using professional judgment, EPA assumes that respirator use is unlikely for the installation and demolition of XPS/EPS Insulation in Table 4-13.

Systematic Review – Public and Peer Review Comments
Charge Question 2.1: Please comment on the approaches and/or methods used to support and inform the gathering, screening, evaluation, and integration of data/information used in the Draft Risk Evaluation for Cyclic Aliphatic Bromide Cluster (HBCD). **Charge Question 2.2:** Please also comment on the clarity of the information as presented related to systematic review and suggest improvements as warranted.

#	Summary of Peer Review Comments for Specific Issues Related to Charge Question 2	EPA/OPPT Response
Summary of Peer Review Comments for Specific Issues Related to Charge Question 2.1		
Difficulty finding referenced data		
SACC	**SACC COMMENTS:** • Given the length of the various supplemental documents, it was difficult to find reviews of key sources, including ratings of specific interest to specific subject matter experts. Some type of key word indexing of all sources (not just newly added sources) would allow quicker and easier access and greatly improve the ability of peer reviewers to evaluate the quality of EPA's SR. Those review outcomes can reasonably be reported in either supplemental documents (as done for all current evaluations) or online, as long as clear links and indexing are provided. (p. 96)	EPA appreciates the suggestions and is continuing to refine its Systematic Review protocol. In addition, EPA is seeking feedback from the National Academies of Science (NAS) on its Systematic Review process, including data evaluation criteria and data quality rating methods used in TSCA Risk Evaluations. The NAS webinars took place from June through August 2020. EPA will consider all comments and feedback received in updating its protocol.
SACC	• One member suggested that the SR process would benefit by application of either a condensed data quality scoring system (*e.g.,* Klimisch et al., 1997) for each studying including those identified in the initial literature survey that were excluded from further consideration or by following the National Toxicology Program's (NTP) Center for the Evaluation of Risks to Human Reproduction (CERHR) method (*e.g.,* Chapin et al., 2008). (p. 96)	
SACC	• Members generally agreed that prior evaluations that are foundational should be explicitly identified, and justification of their inclusion should be provided either individually or as a group. Specifically, prior studies that form the basis of a "systematic review" (*i.e.,* that introduces a collection of sources that are included in subsequent analyses, but which essentially bypass steps in the TSCA SR), should themselves display the critical characteristics of an SR. It may be reasonable to accept the utility of older sources based on previous evaluations, but this should be explicitly shown in the flow diagram describing the Evaluation's SR. (p. 96)	
SACC	• It is important to distinguish between a source that has been critically reviewed by this TSCA SR protocol and from sources included as part of a "legacy" determination. At least one member suggested that, given the two-tiered nature of the SR process, it might be better to refer to current efforts as a "limited SR," or if justified, an "updated SR." Another member suggested that sources	

SACC	identified in prior reviews by bodies judged "authoritative" (*e.g.,* IARC, IPCS, ATSDR) might be assigned higher status and subjected to less scrutiny than previously unreviewed sources. (pp. 96-97) • One member suggested that EPA submit its methodology to a peer reviewed journal for further vetting (p. 96) and obtain further peer review feedback and/or support for use of EPA's TSCA specific SR process. (p. 98). This approach might be more rapid than attempting to obtain a review by the National Academy of Sciences (NAS) as previously recommended. (p.96) • As it has been done in previous TSCA chemical reviews, the Committee recommended EPA revise its TSCA systematic review (SR) protocol/practice and take a more systematic and more complete approach to reviewing the available information sources and data. EPA is encouraged to move forward with adopting a review protocol that is more explicit, more systematic and more objective than the current TSCA SR protocol. An overview of current SR best practices was presented during the public comments13. The empirical approach proposed by Woodruff and Sutton (2009) forms the basis for the approach adapted by the National Toxicology Program's Office of Health Assessment and Translation (OHAT) in 2013, reviewed by the National Academies, and adopted by EPA's Integrated Risk Information System's Review (IRIS). Recently, Singla et al., (2019) identified several best practices for systematic review that TSCA should adopt. It is expected that the identified practices will be consistent with EPA's TSCA evaluation needs. Should TSCA mandates necessitate specific modification to current best practices, for example the IRIS SR protocol, these modifications should undergo peer-review and then clearly explained to the SACC. (pp. 151-152)	
Inclusion and exclusion rationale		
SACC	**SACC COMMENTS:** • At a minimum, clarity of the SR in the Evaluation would be improved by providing a brief statement explaining the reasons for inclusion or exclusion of each source in subsequent analyses. (p. 96) • Use of prior reviews should also not preclude examination of newer literature. (p. 96)	EPA published the *Strategy for Conducting Literature Searches for HBCD* in June 2017 along with the scope document for HBCD, similar to all first 10 TSCA chemical risk evaluations. This document outlined the literature search strategy and title/abstract inclusion/exclusion criteria used for screening, found in Appendix E.

		EPA relied on previous assessments (*e.g.,* IRIS) for identifying relevant literature in addition to the literature search that EPA performed in February 2017, as described in the aforementioned *Strategy for Conducting Literature Searches for HBCD.* EPA also considered new literature when it was reasonably available.
SACC	**SACC COMMENTS:** • The Committee recommended that all sources reporting estimates of physical-chemical properties be subjected to the same TSCA SR criteria as are other sources. The chemical property data (Section 1.1) appear in the Evaluation prior to discussion of Systematic Review (Section 1.5). This gives the impression that the selection and review of sources reporting chemical property estimated values occurs outside of the TSCA SR process. (p. 97) • The Committee expressed concern that estimates obtained or derived from the chemical property literature are often adopted from a single source without determining whether the value is supported by other studies. (p. 97)	All chemical properties values used in the risk evaluation, whether measured or estimated, were subject to data evaluation using systematic review criteria. Values from studies rated high for data quality were used preferentially and no values from unsatisfactory studies were used. The data quality evaluation results for physical chemical properties have been added as a supplemental file.
Data Gathering		
SACC	**SACC COMMENTS:** EPA has novel mechanisms available to request information from industry under the revised TSCA and should request import and use information from known and suspected users of HBCD within the time of the risk evaluation. (p. 100) • The Committee suggested that EPA re-query the DataMyne database to ensure imports have ceased or to account for the "missing" Dow imports. Depending on the result, EPA may reconsider its confidence that dependence on this information as complete is a conservative overestimate. (p. 100) • For example, Dow Chemical imported 48 Metric Tons (MT) (105,822 pounds) in 2017 and reported having a stockpile of 41 MT (90,389 lbs.) in	When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation. EPA looked at reasonably available information and determined that there are no reliable sources of information on small quantities of HBCD that are imported or used by processors. EPA re-queried Datamyne and found no HBCD imports, but the database

	2018. Is it assumed that all of this material has now been processed? (p. 101) • Therefore, there seems to, in fact, be some uncertainty around how much HBCD is in stockpiles, in use, or in disposal, and calls into question the EPA assumption that given almost all use of HBCD has ceased, exposures to humans and the environment from legacy uses will slowly be reduced. As a result, and as requested above, current, ongoing and future monitoring is critical for supporting and validating EPA assumptions and modeling predictions used in this Evaluation. EPA may also reconsider its confidence that dependence on this information as complete is a conservative overestimate. (p. 101)	aggregates bills of lading and does not correct for any errors in the underlying data. For the volumes imported by Dow Chemical in 2017, EPA confirmed with company representatives that all of the HBCD was processed into XPS foam. In addition, the release information reported to TRI program from Dow Chemical was incorporated into the release assessment for the Processing of HBCD powder to produce XPS foam (see Section 2.2.5). EPA has added details to Section 1.2 concerning the potential for stockpiles to result in additional exposures. The HBCD Risk Evaluation included an assessment of background exposures based on biomonitoring and environmental monitoring data that incorporate any and all exposures including those from historical releases from facilities releasing to the environment (*e.g.,* via water or air) (Section 1.2.9).
SACC	**SACC COMMENTS:** • Implement procedures to require manufacturers and users to provide the data on activities, uses, emissions, and disposal needed to perform a robust risk assessment. (p. 115)	EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to complete the HBCD risk evaluation using a weight of scientific evidence approach in light of the limited time available under the statute for completing the risk evaluation. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and

		synthesize for use in risk evaluations, considering the deadlines for completing the evaluation.
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 2.2**	**EPA/OPPT Response**
Clarifications		
SACC	**SACC COMMENTS:** • EPA's overall strategy is described in the Application of Systematic Review in TSCA Risk Evaluations which is referenced in the Evaluation. However, there should be enough explanation of the SR process in the Evaluation to allow the reader to proceed without first reading the SR methodology document in its entirety. (p. 97)	The systematic review process is explained broadly in Section 1.5. Additionally, details about data evaluation and study selection are described in the individual Approach and Methodology sections of the final risk evaluation.
SACC	**SACC COMMENTS:** • Excluded studies, as well as cited/included studies, should be enumerated. (p. 97)	Excluded studies are enumerated in the literature flow diagrams in Section 1.5.1.
SACC	**SACC COMMENTS:** • A summary of the findings placed at the beginning or end of each section would be helpful. (p. 97)	EPA has improved section summaries where possible and will consider further improvements to the risk evaluation format for future evaluations.
Recommendations to improve the general TSCA SR		
SACC	**SACC COMMENTS:** • Establish an indexing system to facilitate searching for both cited/included and excluded studies. (p. 98)	EPA will consider an indexing system for future evaluations. See interactive HAWC trees in scopes of next 20 high priority chemicals.
SACC	**SACC COMMENTS:** • When prior reviews conducted by the EPA or other regulatory and non-regulatory agencies are integrated into a current review, EPA should explain why those prior reviews are viewed as methodologically equivalent to the approaches specified in the Application of Systematic Review in TSCA Risk Evaluations. (p. 98)	EPA used previous chemical assessments to quickly identify relevant key and supporting information as a pragmatic approach to expedite the quality evaluation of the data sources; many of those data sources were already captured in the comprehensive literature search performed according to *Strategy for Conducting Literature Searches for Cyclic Aliphatic Bromine Cluster (HBCD).* EPA has revised its searching and screening procedures to include all studies in the systematic review process (screening, data

		evaluation) for the next set of TSCA chemical risk evaluations.
SACC	**SACC COMMENTS:** • When prior chemical assessments conducted by the EPA or other regulatory and non-regulatory agencies are used to identify key information, those assessments should be updated to ensure new information sources are not excluded. (p. 98)	EPA relied on previous assessments (*e.g.,* IRIS) for key information but also reviewed relevant literature identified in the literature search that EPA performed.
SACC	**SACC COMMENTS:** • The Populations, Exposures, Comparators, and Outcomes (PECO)) statements, including inclusion and exclusion criteria, for chemical properties should be distinguished from other problem formulation statements (*e.g.*, human health toxicity, exposure environmental toxicity, etc.). (p. 98)	PECO and PESO statements are included in appendix E of the Problem Formulation. The Problem Formulation is referenced in the Risk Evaluation with a hyperlink to the PDF.
Recommendations to improve the HBCD SR		
SACC	**SACC COMMENTS:** • As stated in Section 3.2 Human Health Hazards "EPA considered studies of low, medium, or high confidence for hazard identification (ID) and dose-response analysis. Information from studies that were rated unacceptable were only discussed on a case-by-case basis for hazard ID and weight-of-evidence assessment but were not considered for dose-response analysis. EPA considered the specific reasons for the unacceptable scoring in determining whether unacceptable studies could remain useful for hazard ID or weight-of-evidence." EPA should explain how this language is consistent with screening techniques for data exclusion described in Section 1.5 of the Draft Risk Evaluation for Cyclic Aliphatic Bromide Cluster (HBCD). (p. 98)	EPA published the title/abstract inclusion/exclusion criteria for HBCD in Appendix E of the Strategy for Conducting Literature Searches for Cyclic Aliphatic Bromine Cluster (HBCD) and inclusion/ exclusion criteria statements used during full text screening in an appendix to the problem formulation document for HBCD. Data quality criteria used for scoring each discipline are provided in a separate document titled Application of Systematic Review in TSCA Risk Evaluations, which also outlines evidence integration strategies that will be further developed for the next risk evaluations. Screening for relevance based on inclusion/exclusion criteria is an independent step from the data quality evaluation.
SACC	**SACC COMMENTS:** • In chemical property value selection, higher weight should be assigned to experimental data (see Cumming and Rucker 2017) from primary references than to secondary sources (*e.g.,* Hansch et al., 1995) or modeled estimates	EPA agrees measured values from reliable studies are preferred over estimated values. The Cumming and Rucker citation did not contain

	(*e.g.*, Epi Suite™). (p. 98)	any data for HBCD.
#	**Summary of Public Comments for Specific Issues Related to Charge Question 2**	**EPA/OPPT Response**
General		
44 59 31,51 31,51,59 31,51 31,51 31, 51 31,51	**PUBLIC COMMENTS:** • Protocols should be created for all review components before conducting the review to minimize bias and ensure transparency in decision making, specified as best practice by all established methods. • A non-empirically based "scoring" system does not align with best practices. o EPA should not use a quantitative scoring method to assess quality in individual studies. o EPA must be careful not to conflate study reporting with study quality. o EPA should not exclude otherwise quality research based on a single reporting or methodological limitation. o EPA should employ a scientifically valid method to assess risk of bias of individual studies. • EPA should consider the possibility of publication bias in the peer-reviewed literature; *i.e.*, the possibility that studies with negative findings may not have been published. • Several methodological changes were applied that have not been peer-reviewed. No rationale for these changes was provided. • EPA should update the general systematic review guidance document to reflect any broadly applicable changes and add additional information as it is developed. Additions include a description of the standardized procedures that will be used to integrate evidence to ensure consistent use of best available science, weight of the scientific evidence, and, as applicable, understanding of the mode of action (MOA). • The draft TSCA systematic review guidance document must undergo peer review before risk evaluation documents are drafted. • The chemical-specific systematic review protocol should be published during scoping. • EPA should describe efforts undertaken to calibrate the reviews of different reviewers, as there are inconsistencies in data quality evaluation both within and across chemicals. o EPA should ensure that staff doing the data quality evaluations	EPA published the title/abstract inclusion/exclusion criteria for HBCD in Appendix E of the Strategy for Conducting Literature Searches for Cyclic Aliphatic Bromine Cluster (HBCD) and inclusion/ exclusion criteria statements used during full text screening in an appendix to the problem formulation document for HBCD. Data quality criteria used for scoring each discipline are provided in a separate document titled Application of Systematic Review in TSCA Risk Evaluations, which also outlines evidence integration strategies that will be further developed for the next risk evaluations. Screening for relevance based on inclusion/exclusion criteria is an independent step from the data quality evaluation. TSCA directs that EPA consider reasonably available data. EPA is unable to consider the potential for negative data that is not reasonably available. EPA appreciates the suggestions and is currently in the process of refining its Systematic Review protocol. In addition, EPA is seeking feedback from the National Academies of Science (NAS) on its Systematic Review process, including data evaluation criteria and data quality rating methods used in TSCA Risk Evaluations. The NAS webinars are currently scheduled from June through August 2020. EPA will consider all comments and feedback received in updating its protocol.

	have the appropriate subject matter expertise and also train staff on general data quality review methods. o EPA should also describe efforts being made to do internal quality checks on the data quality evaluations for individual studies and risk evaluations.	
Data Gathering		
28,33,48 31,51 44 31,51 41	**PUBLIC COMMENTS:** • TSCA law authorizes EPA to require testing to develop data about health, environmental effects, and/or exposure when there are insufficient data to determine whether a chemical substance or mixture presents an unreasonable risk to human health or the environment. EPA did not use its authority to fill identified data gaps. o It is expected that the agency would take advantage of this authority and conduct a testing/research needs assessment in concert with its prioritization and evaluation programs so that any filling of data gaps would be completed BEFORE a Risk Determination is attempted. o To date, there is no evidence of any EPA requests for generation of additional data under TSCA section 4 despite the significant data gaps on chemicals on which risk evaluations are being conducted. o EPA should detail how it plans to fill the numerous information data gaps. • EPA must be clear and specific about its use of information from other assessments. • The review of HBCD under TSCA should utilize all of the materials developed by the Integrated Risk Information System (IRIS) program before the assessment was transferred to the TSCA program. • EPA should consider "grey" literature, such as technical reports, unpublished industry data, and studies generated for regulatory purposes at the data collection stage. • EPA relies on assurances that HBCD is no longer made in certain facilities, not likely to be made by small facilities that are not required to report, and not made by other countries and imported. o Self-reported information from manufacturers may misrepresent true levels. o EPA should use its authority to obtain additional information from manufacturers on how much HBCD is produced/imported. o The draft risk evaluation states that that 171 of 188 Parties to the Stockholm convention on Persistent Organic Pollutants have agreed to	The reasonably available information for each chemical substance allowed EPA to complete the risk evaluation and determine whether the chemical substance presented an unreasonable risk under the conditions of use. In some cases, when information reasonably available to EPA was limited, the Agency relied on models; the use of modeled data is in line with EPA's final Risk Evaluation Rule and EPA's risk assessment guidelines. EPA considers reasonably available data on a chemical by chemical basis and would exercise any necessary information gathering in a fit-for-purpose manner, as was the case for PV29. As part of the consideration of reasonably available information, EPA considers data gaps and the need for additional information as appropriate. EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to complete the HBCD risk evaluation using a weight of the scientific evidence approach in light of the limited time available under the statute for completing the risk evaluation. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development.

	ban the production, use, import, and export of HBCD, but does not mention which countries have not agreed. ○ It also mentions that only three Parties have registered for an exemption for production for expanded polystyrene (EPS) and extruded polystyrene (XPS) in buildings but does not mention that one of the three countries is China and that none of them report the volumes they are producing or using.	EPA conducted extensive and varied data gathering activities for each of the first 10 chemicals including extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports, outreach meetings, searches of internal EPA databases, and more. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation.
Modifications to Systematic Review		
59 31,51 59	**PUBLIC COMMENTS:** • The new approach relies on "key and supporting/ influential information." EPA must be clear in the approach and criteria used to identify key studies and must specify how these studies were evaluated. ○ This approach was not previously published nor peer reviewed, has not gone through a public comment period, and does not meet the requirements of EPA's regulations. ○ EPA does not provide clear criteria to identify what "influential information sources" are. ○ EPA does not explain what "key" data are in the phrase – 'evaluated the confidence of the key and supporting data'. • The new approach uses a "hierarchy of preferences" to exclude relevant studies rather than considering all the relevant science. ○ Data for occupational exposures which are rated 'acceptable' by the TSCA method were excluded. • Instead of the current method, EPA should use a peer-reviewed, validated systematic review method for chemical evaluations.	The systematic review approach, including the use of prior assessments, is described throughout the risk evaluation including the Executive Summary, Section 1.5, and Section 3.2.1. For releases and occupational exposures, the hierarchy of preferences is described in Appendix E.7 of the Risk Evaluation for HBCD. EPA's consideration of data, including data that was not incorporated into the evaluation of releases to the environment and occupational exposure based on the hierarchy of preferences, is discussed Sections 2.2 and 2.4.1 of the Risk Evaluation for HBCD. EPA appreciates the suggestions and is currently in the process of refining its Systematic Review protocol. In addition, EPA is seeking feedback from the National Academies of Science (NAS) on its Systematic Review process, including data evaluation

		criteria and data quality rating methods used in TSCA Risk Evaluations. The NAS webinars are currently scheduled from June through August 2020. EPA will consider all comments and feedback received in updating its protocol.
Issues with Data Quality Evaluation Metrics in Regard to Epidemiological Studies		
59 59	**PUBLIC COMMENTS:** • The revised criteria for evaluating the quality of epidemiological studies make it more likely that relevant epidemiological studies will be excluded. o Metric 1: Studies can still be scored low for reporting reasons. o Metric 2: EPA removed references to the STROBE guidelines and no longer allows a study to be excluded on reporting grounds (though it can still be scored Unacceptable for substantive reasons relevant to this metric). o Metric 3: EPA kept STROBE references but added an additional requirement to be scored Unacceptable: "Potential differences in exposure groups [or case and control groups, depending on study type] were not controlled for in the statistical analysis." o Metric 4: The criteria added to ensure that a study scores high is quite restrictive. o Metric 5: Now, cannot score as high and the criteria for medium scoring are much more involved. o Metric 6: EPA changed "not reported" to "not sufficiently reported" to receive a score of Unacceptable. Based on sufficiency this may lead to more epidemiological studies being binned as unacceptable instead of low. o Metric 10: This change was appropriate. o Metric 11: Cannot score High, also cannot score Unacceptable. A study that would previously be scored High would now be Medium; a study that would have scored Unacceptable would now be Low. The descriptions are identical to the original ones, just shifted to the new score. o Metrics 12-15: EPA is unilaterally making it more difficult for epidemiological studies to score High on the quality metrics. o Metric 14: EPA has changed the scoring for this metric so that it can no longer be scored High, only Medium or Low. The previous description for High is now the description for Medium, with slight revisions; it now reads, "The description of the analysis is sufficient to understand precisely what has been done and to be conceptually reproducible with access to the analytic data."	EPA/OPPT's quality evaluation method was developed following identification and review of various published qualitative and quantitative scoring systems to inform EPA's own fit-for-purpose tool. The development process involved reviewing various evaluation tools/frameworks (*e.g.,* OHAT Risk of Bias tool, CRED, etc.; see Appendix A of the Application of Systematic Review in TSCA Risk Evaluations document and references therein), as well as soliciting input from scientists based on their expert knowledge about evaluating various data/ information sources specifically for risk assessment purposes. The epidemiologic criteria were later revised to more stringently distinguish between High, Medium and Low studies. After additional piloting of the criteria, EPA found that the initial iteration of the epi data quality criteria (as published in the Application of Systematic Review in TSCA Risk Evaluations) was inadvertently skewing quality scores toward the tail ends of the scoring spectrum (High and Unacceptable). To have the criteria represent a more accurate depiction of the quality levels in the epi literature, the criteria were revised using 2 methods. The first method was to make the unacceptable

	○ Metrics 16-17 and 19: EPA inappropriately applies an adverse outcome pathway (AOP) standard to effect biomarkers. ○ Metric 18: Studies cannot be given scores of High or Unacceptable, only Medium or Low. ○ Metrics 19-22: Studies cannot be given scores of Unacceptable. • The SACC should provide feedback on the proposed updated criteria for evaluation of epidemiology studies.	metrics less stringent. This was accomplished by either rewording the metrics to allow for more professional judgment in the interpretation of the unacceptable criterion, or in some cases, completely removing the unacceptable bin from metrics that EPA determined were not influential enough to completely disqualify a study from consideration (mostly metrics in the Analysis and Biomonitoring domain). EPA found that these criteria changes greatly reduced the type one error in the Unacceptable scoring. No acceptable studies were inaccurately classified as Unacceptable. The second method was to reduce the number of studies that received an overall High rating. The majority of overall scores in EPA's initial evaluations during piloting tended to be High. Therefore, EPA strived to revise the criteria to provide more gradation in the scoring to more accurately and objectively distinguish studies of the highest quality from medium and low-quality studies. To do this, EPA removed the High criterion from some metrics, particularly in dichotomous metrics (High/Low or High/ Unacceptable) that were primarily being binned as High by reviewers across most of the studies. These dichotomous metrics were contributing to the overall quality scores being skewed towards High. To address this, EPA shifted some of the dichotomous metrics such that the highest metric score possible (for all studies) is a Medium. The change led to the dichotomous metrics having less significant impact to the numerical scoring and the overall quality rating for each study. With the changes to the criteria, EPA observed fewer studies with Unacceptable ratings and

		more studies shifting from High to Medium, with only the highest quality studies receiving a High overall rating. Out of the ~200 relevant epidemiologic studies and cohorts evaluated for data quality for the first 10 TSCA chemicals, the majority (~80%) still scored as High or Medium. The remaining ~20% of studies scored Low or Unacceptable. EPA is confident that no studies of acceptable quality were inappropriately assigned as Unacceptable. EPA is also confident that the revised criteria bins the quality levels of these epi studies more appropriately than the previous iteration. Additional refinements to the epidemiologic data evaluation criteria are likely to occur as EPA's validation and process improvement efforts continue.
Clarification		
59	**PUBLIC COMMENTS:** • EPA indicates that the "key/supporting data sources" "…allowed EPA to maximize the scientific and analytical efforts of other regulatory and nonregulatory agencies by accepting for the most part the relevant scientific knowledge gathered and analyzed by others except for influential information sources that may have an impact on the weight of the scientific evidence and ultimately the risk findings…" o EPA should explain what is meant by "accepting for the most part." o Without more information, it could appear that EPA is accepting certain conclusions for expediency based on political or other pressures, while subjecting other conclusions considered unfavorable to further scrutiny. o Evidence should be identified first and then used to determine the conclusions not the other way around. o EPA should publish and adhere to a protocol with clearly defined criteria to ensure consistent identification and evaluation of evidence. A protocol will ensure that EPA's process is replicable and transparent.	EPA appreciates the suggestions and is currently in the process of refining its Systematic Review protocol. In addition, EPA is seeking feedback from the National Academies of Science (NAS) on its Systematic Review process, including data evaluation criteria and data quality rating methods used in TSCA Risk Evaluations. The NAS webinars are currently scheduled from June through August 2020. EPA will consider all comments and feedback received in updating its protocol.
31,51	**PUBLIC COMMENTS:** • More detail and specificity on the data integration approach used are needed.	In response to comments, EPA has made several editorial changes to increase the

	○ The approaches for evaluation of consistency, relevance, coherence, and biological plausibility are not clearly documented. ○ While EPA discusses consistency, relevance, coherence, and biological plausibility in some parts of the risk evaluation, EPA should more clearly and fully articulate how these factors are integrated to inform hazard and exposure assessments, as well as the risk characterization. These data integration discussions should be cited in the risk determination.	transparency of its systematic review process and methodologies used. In addition to the data evaluation criteria published in the *Application of Systematic Review in TSCA Risk Evaluations*, EPA included the data integration strategy in Appendix E.7 that EPA used to integrate environmental release and occupational exposure data.
59	**PUBLIC COMMENTS:** • The 'hierarchy of preferences' does not have a valid empirical basis and by excluding relevant studies, EPA is introducing bias into its evaluations. There is also a lack of transparency in how the hierarchy was applied and which sources were ultimately excluded on this basis, which is inconsistent with the basic premise of a systematic review. ▪ For example: EPA stated that there were 42 sources rated as unacceptable, however within EPA's supplemental rating sheets we found 47 sources (based on unique Hero ID) or 74 individual entries that were rated as unacceptable. The lack of alignment and clear protocol made it impossible to identify the stated 36 sources that may have been eliminated due to the 'hierarchy of preferences' EPA introduced. • It difficult to identify what the key sources of data and information are; a clearly marked list of these sources should be presented in the draft risk evaluations. ○ EPA identifies 11 'key sources' with 15 additional sources (26 total) used for data integration for environmental releases and occupational exposure data sources. But the corresponding table in Appendix E7, Table E-13, contains 30 entries, with the majority being listed as excluded, so it is unclear what the 26 sources EPA used are, and which of these are the 11 "key" sources. EPA should revise this table to be more transparent, and clearly list the studies included and considered "key."	The hierarchy of preferences used for releases and occupational exposures is described in Appendix E.7 of the Risk Evaluation for HBCD. EPA's consideration of data, including data that was not incorporated into the evaluation of releases to the environment and occupational exposure based on the hierarchy of preferences, is discussed in Sections 2.2 and 2.4.1 of the final Risk Evaluation for HBCD. EPA discusses the selection of key/supporting sources for each scientific discipline–specific evidence supporting the Risk Evaluation in Section 1.5.1. The integrated sources and data used to support human health and environmental risk of HBCD are specifically cited throughout the HBCD risk evaluation. For clarification on the examples provided, the 42 unacceptable sources reported in the HBCD literature flow diagram for environmental releases and occupational data sources are based on sources where all extracted data from the source was rated unacceptable. A data source may contain multiple data points or sets or information elements that individually received ratings based on the data evaluation criteria. A source can be considered an acceptable source in the literature flow diagram if it contained an extracted data that was rated acceptable.

		The table in Appendix E7, Table E-13, is specific to identified occupational monitoring data on HBCD and is not representative of all of the sources included in the literature flow diagram for Environmental Releases and Occupational Exposure.

Environmental Fate and Transport – Public and Peer Review Comments (within Comment text; contractor's paraphrased recommendation in bold)		
Charge Question 3.1: Please comment on the use of field measured BAF values for upper trophic level fish from (He et al., 2013) and (Wu et al., et al., 2010) for use in assessing human or wildlife exposure via fish ingestion. **Charge Question 3.2:** Please provide any specific suggestions or recommendations for alternate approaches that could be considered for accounting for bioaccumulation of HBCD into food webs/diet of humans or wildlife. **Charge Question 3.3:** Please also comment on the use of the BAF data from Chinese predatory fish species to address human exposure via fish ingestion. **Charge Question 3.4:** Please provide any specific suggestions or recommendations for alternate approaches to derive media specific degradation half-lives for use in exposure assessments from data sets where values for the same environmental fate endpoint (*e.g.*, biodegradation half-life in aerobic soil) vary widely.		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 3**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 3.1		
Recommended approach modifications		
SACC	**SACC COMMENTS:** • Evaluate how uncertainty in HBCD water solubility and other variables that form the basis of models impact the uncertainty in exposure estimates. (p. 110)	Water solubility over the reported ranges had little impact since most of HBCD partitions to sediment. A sensitivity analysis was conducted for biodegradation half-life impact on water column and sediment concentrations. EPA reviewed the input variables to the exposure models used for exposure estimates and selected values from studies of acceptable quality where uncertainties in measured values were minimized.
SACC	**SACC COMMENTS:** • Consider the long in-service lives and long environmental half-lives of HBCD products as a major HBCD legacy environmental deposit reservoir and incorporate this source of HBCD persistence in the	In several ways, EPA considered HBCD's persistence in products with long in-service lives and the environment. EPA assessed aggregate background concentrations of HBCD caused by releases that occurred in the past. These releases result in potential human and environmental exposure to HBCD, and EPA assessed the

	assessment of exposure pathways. (p. 110)	risks resulting from these potential exposures, considering half-lives in the environment. EPA also evaluated risks of exposure to HBCD in products after they are produced, including occupational risks from demolishing buildings that have HBCD-containing insulation, risks of workers in facilities that recycle electronics products; and risks of commercial and consumer uses as well as disposal of products.
SACC	**SACC COMMENTS:** • Incorporate exposures from imported products as a source of new HBCD introductions to the U.S. (p. 110)	Exposures from use of Imported EPS Resin Beads during processing are assessed as outlined in Section 1.4.
SACC	**SACC COMMENTS:** • The EPA could also collaborate with the National Oceanic and Atmospheric Administration (NOAA) on its Status and Trends Program. Some elements of that program have already added HBCD to their analyte list. (p. 110)	EPA conducted extensive data gathering activities for HBCD and the other 9 chemicals, including outreach with other State and Federal Agencies. In some cases, when information available to EPA was limited, the Agency relied on models; the use of modeled data is in line with EPA's final Risk Evaluation Rule and EPA's risk assessment guidelines. EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to complete the HBCD risk evaluation using a weight of the scientific evidence approach in light of the limited time available under the statute for completing the risk evaluation. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation.
Panel Recommendations on Evaluation text (Listed)		
SACC	**SACC COMMENTS:**	Section 2.1 refers to Fate and Transport and is not

	• Add to Section 2.1: "Considerable amounts of polystyrene board may be lost or improperly discarded directly into the environment. The General Public typically considers polystyrene board to be harmless and handles and disposes of it without thought for its potential to contaminate the environment. For example, such board (included recycled material) has been used in arts & crafts, and even for insulation in beehives (see for example www.youtube.com/watch?v=egix-XrxDKk)." (p. 111)	relevant to discussions of environmental releases or exposures. Polystyrene resin is already assessed as an occupational exposure scenario. Additionally, background environmental and general population exposures are independently assessed, which incorporates exposures from all sources including potential remnants of polystyrene boards.
SACC	**SACC COMMENTS:** • Add to Section 2.1.2, Table 2.1: Introduce a new property "Photolysis and hydrolysis" with value "HBCD is an acknowledged high production volume, PBT chemical. Estimation of HBCD photolysis and hydrolysis seems to be an unnecessary and possibly problematic shortcut as these tests are fairly straightforward." (p. 111)	The production volume and PBT characteristics of HBCD are discussed in Section 1.2 Uses and Production Volume, and 2.1.2.7 PBT Characterization in the RE. Table 2.1 is reserved for reporting specific environmental fate endpoints.
SACC	**SACC COMMENTS:** • Add to Section 2.1.2, Table 2.1, last line, include the BCF value for whole fish to in the value text, given it is likely what wildlife consume the whole fish. Indicate in the text if these BCFs are calculated on a wet weight or lipid basis. (p. 111)	The tables have been edited where sufficient information was reasonably available.
SACC	**SACC COMMENTS:** • Note in Sections 2.1.2.2 and 2.1.2.3 that the presence of HBCD with the polymer matrix (*e.g.*, polystyrene) will drastically alter fate. (p. 111)	EPA discussed the uncertainty associated with the behavior of HBCD within a polymer matrix in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport.
SACC	**SACC COMMENTS:** • Add to Section 2.1.2.4: "WWTP removal processes will be a function of treatment steps applied. Some U.S. WWTPs (*e.g.*, San Diego, as well as several facilities discharging in Maine and Alaska) receive waivers to practice less stringent treatment and thus may have lower HBCD removal rates than described in the Ichihara et al., (2014) citation." (p. 111)	EPA agrees. Exposure assessments in the risk evaluation included 0% removal which would cover the facilities with waivers.
SACC	**SACC COMMENTS:** • Add to Section 2.1.2.4: "The density of polystyrene itself ranges from	EPA incorporated this general discussion into Section 2.1.2.4. However, the commenter did not provide

	0.96 to 1.04 (g/cm3). This is close to neutral buoyancy. Therefore, its removal during wastewater treatment may be straight-forward. Biofilm formation on the surface of fragments and flocculation may facilitate sinking and removal in the solids. Voids in polystyrene foam will cause it to float and allow removal by skimming, but fragments may become waterlogged over time." (p. 111)	references to permit data quality evaluation and incorporation of the exact language.
SACC	**SACC COMMENTS:** • In Section 2.1.2.6: In reference to the EPA cited Lindberg et al., et al. (2004) study showing only 150 to 250 ng/g lipid in Swedish falcons, Guerra et al. (2012) observed a maximum level ~100 times higher in Canadian falcon eggs. (p. 111)	EPA cited (Lindberg et al. 2004) as evidence of bioaccumulation in terrestrial food chains. Discussion of Guerra et al., (2012) was incorporated into Section 4.3.1 Assumptions and Key Sources of Uncertainties for the Environmental Risk Characterization in the context of the uncertainty of the likelihood of sex-specific transfer of HBCD to offspring. The calculations used to predict HBCD trophic transfer for both the aquatic and terrestrial predators are provided in Appendix H.2. Estimations for HBCD trophic transfer are presented in Table 3-2. Were calculated using exposure factors from the *U.S. EPA Wildlife Exposure Factors Handbook* (U.S. EPA, 1993b) and HBCD biomonitoring data.
SACC	**SACC COMMENTS:** • In Section 2.1.3, paragraph 3: Provide specific supporting reference(s) for the statement "Half-lives estimated from studies ranged from days to greater than 6 months." (p. 111)	EPA provides the references in the full discussion Appendix C. Fate and Transport C.1. Biodegradation.
SACC	**SACC COMMENTS:** • In Section 2.1.3, paragraph 3: Provide references for the statement "…environmental monitoring showing the presence of HBCD in dated sediment cores it can be concluded that HBCD is persistent in the environment." (p. 111)	EPA has added the reference below: Drage, D; Mueller, JF; Birch, G; Eaglesham, G; Hearn, LK; Harrad, S. (2015). Historical trends of PBDEs and HBCDs in sediment cores from Sydney estuary, Australia. Sci Total Environ 512-513: 177-184. http://dx.doi.org/10.1016/j.scitotenv.2015.01.034. (Drage et al. 2015)
SACC	**SACC COMMENTS:** • In Section 2.1.3, paragraph 7: Provide references for the statement "…the reported dissolved HBCD concentrations in Chinese water bodies were in the range of 0.04 to 0.06 ng/L. These are about an order of magnitude lower than the range of dissolved HBCD surface	EPA has added the references below: Wu, JP; Guan, YT; Zhang, Y; Luo, XJ; Zhi, H; Chen, SJ; Mai, BX. (2010). Trophodynamics of hexabromocyclododecanes and several other non-PBDE brominated flame retardants in a freshwater food web.

	water concentrations reported in surface water monitoring studies." (p. 112)	Environ Sci Technol 44: 5490-5495. (Wu et al. 2010) He, MJ; Luo, XJ; Yu, LH; Wu, JP; Chen, SJ; Mai, BX. (2013). Diasteroisomer and enantiomer-specific profiles of hexabromocyclododecane and tetrabromobisphenol A in an aquatic environment in a highly industrialized area, South China: vertical profile, phase partition, and bioaccumulation. Environ Pollut 179: 105-110. (He et al. 2013)
SACC	**SACC COMMENTS:** • In Section 2.1.3, paragraph 7: Provide references for the statement "Using available data, an upper trophic level lipid normalized field measured BAF (northern snakehead) was selected for use as a surrogate species for the fish ingestion exposure assessment." (p. 112)	A reference is not required for the quoted text.
SACC	**SACC COMMENTS:** • In Section 2.1.3, paragraph 7: Provide references for the statement "the limited number of species and field conditions add to uncertainty associated with the use of these BAFs in estimating human exposure to HBCD via fish ingestion." (p. 112)	A reference is not required for the quoted text.
SACC	**SACC COMMENTS:** • Add to Section 2.1.3, last paragraph, add discussion on the issue that alternatively, the simplest approach may be to use field measurements in fish via EPA Lake, River & Streams Programs. However, at present HBCD was not included in the analyte list of these programs. Residual tissue aliquots may have been stored. (p. 112)	EPA did not add this discussion because no data on HBCD concentrations were found in the suggested data sources.
SACC	**SACC COMMENTS:** • In Section 2.1.3, page 70 EPA identified two BCF studies and two BAF studies on HBCD. BAF studies are preferred over BCF studies because they represent exposure of the organism to HBCD via all routes, including diet which is important for a hydrophobic chemical such as HBCD. (p. 112)	The subject text now appears in Section 2.1.2.6 Bioaccumulation/Bioconcentration. The language of the full paragraph explains the rationale for the preferential use of BCF over BAF in the context of this RE.
Panel Recommendations (within preface to committee response text)		

SACC	**SACC COMMENTS:** • It appears likely that some HBCD-containing electronics may still be imported into the U.S. Given this situation, the primary "condition of use" concern should be exposures from in-use products and the fate and disposal of these products after useful service life. (p. 101)	As stated in Section 1.2.5.3 Solder Paste, while one company uses HBCD as a fluxing aid in solder paste, which it supplies to electronics manufacturers for use on circuit boards in China, EPA could not confirm that those HBCD-containing electronics are currently imported back into the United States. In addition, EPA expects that HBCD will degrade during the use of the solder paste. Therefore, EPA opted to exclude disposal of these products from the COU.
SACC	**SACC COMMENTS:** • HBCD was until recently added into expanded polystyrene (EPS) and extruded polystyrene (XPS) insulation board as a flame retardant at ~0.5% by weight. This is equivalent to 5 million µg/kg (ppb). Thus, a 1g fragment of polystyrene foam may contain 5,000 µg of HBCD. As a result, considerable HBCD will be transported with these plastic products, and associated debris or polymer fragments into these environments. (p. 102)	EPA agrees that characteristics of the matrix containing HBCD and other factors influence the pathways of exposure and bioavailability of HBCD. The uncertainties in assessing the bioavailability of HBCD, the bioavailability of HBCD in matrices and HBCD in microplastics are discussed in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport.
SACC	**SACC COMMENTS:** • Small plastic fragments (microplastics) <0.5 mm, including polystyrene and associated additives such as HBCD, have been found in drinking waters and in environments all over the world. These findings have raised concern among environmentalists given the risks to human health are not well known. This pathway of exposure is not covered in the HBCD Evaluation and the term "micro-plastics" appears only once (see page 331). "Dust" is discussed multiple times in other sections of the Evaluation, largely in industrial/occupational contexts and, to a lesser extent, in indoor residential exposures. To have a toxic effect, much of the HBCD must move from the polystyrene or other media and reach biological receptors. Thus, consideration of its presence and behavior in such "intermediate" media is critical. (p. 102)	
SACC	**SACC COMMENTS:**	

	• The Committee noted that lack of data regarding bioavailability, form and levels of HBCD (or any other toxicant) in the environment and in humans, can lead to the wrong conclusion. Care must be exercised when coming to conclusions regarding the extent of HBCD (or other toxicant) exposures when there are little data to support assumptions. (p. 103)	
Summary of Peer Review Comments for Specific Issues Related to Charge Question 3.2		
Bioavailability		
SACC	**SACC COMMENTS:** • An HBCD water solubility of 66 µg/L is identified in the Evaluation. This appears to be derived by summing the solubilities of the three individual diastereomers. A concern expressed by the Committee was the limited measurements available for this critical parameter. Subsequent fate/accumulation modeling utilizes this solubility value and incorporates no estimate of variability. Low HBCD water concentrations (low ng/L) are quite difficult to measure accurately. In fact, Table 1 in The Binational Strategy for Hexabromocyclododecane (HBCD) Risk Management (2017) provides an "average" water solubility for the three diastereomers of 0.0034 mg/L (or 3.4 µg/L), 20-fold lower than the value proposed in the Evaluation. In addition, a value from a low of 1.76 to a high of 65.6 µg/L were also observed in Posner et al., (2010). Hence, the estimated concentration in water, which is entered as the BAF denominator, presents a source of uncertainty. The three diastereomers (alpha, beta, and gamma) are present in varying abundances in the HBCD technical mixture, as well as in environmental media and show differences in water solubility and hence may have differing environmental fates. Being hydrophobic, most HBCD released to aquatic environments will associate with organic matter (including microplastics) and not be freely dissolved in water. (p. 104)	EPA agrees that data on water solubility are limited for HBCD and that uncertainty in the water solubility value creates uncertainty in the estimation of fate parameters that use that value. EPA did not use estimated concentrations in water to derive BAFs. BAFs used in the risk evaluation were derived from measured fish tissue concentrations and measured water column concentrations.
SACC	**SACC COMMENTS:** • Consider Committee concerns about differences in HBCD bioavailability ○ Sorption to ambient particulate organic matter, presence in (micro-) plastic debris and association with dissolved organic	EPA discussed the potential impact of HBCD sorption to particulate matter/microplastics on bioavailability in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport.

	matter will reduce apparent HBCD bioavailability. Commonly applied analytical methods (*e.g.*, organic solvent extraction at elevated temperature) do not differentiate the highly bioavailable "dissolved" HBCD fraction from these less bioavailable pools. Hence, the calculated BAFs may be in error. (p. 105)	
Other		
SACC	**SACC COMMENTS:** • It is generally logical to expect that upper trophic level fish (as well as other upper trophic level wildlife, such as otters and birds of prey) will exhibit higher burdens of persistent, hydrophobic contaminants than lower trophic level organisms; a phenomenon known as biomagnification. However, in the citations used in the Evaluation, some lower trophic level organisms exhibited higher burdens. This is discussed further in Question 3.3 below. Caution should be exercised in focusing solely on higher trophic fish species such as the snakehead. (p. 103)	Subsequent to the review of initial RE, a U.S. based study was identified measuring HBCD fish tissue concentrations from sites downstream from point source industrial releases and sites where industrial HBCD releases were not found (Chen et al. 2011). EPA used the highest concentrations in edible fish (carp) from the study to estimate HBCD exposures for subsistence fishers. These concentrations were about 10X greater than those found in Chinese Northern Snakehead, Mud Carp and Suckermouth Catfish (Chen et al. 2011).
Summary of Peer Review Comments for Specific Issues Related to Charge Question 3.3		
BAF data		
SACC	**SACC COMMENTS:** • The BAFs from He et al., (2013) and Wu et al., (2010) have merit for use in estimating (but with unknown certainty) human or wildlife exposure via fish ingestion. However, they involve only two sites and are from samples obtained from a foreign country (southern China), with attendant environmental (*e.g.*, temperature, organic carbon characteristics) and anthropogenic differences (*e.g.*, conditions of use, waste disposal, regulatory restrictions) from the U.S.	EPA discussed this uncertainty in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport
	• The source and form (*e.g.*, polymer/HBCD association) of the HBCD in the Chinese environments in question may not be representative of that commonly occurring in the U.S., where most HBCD has been employed in polystyrene insulation board (the major focus of the Committee's discussion). In contrast, China produces considerable amounts of textiles and electronics, which may contain, or might have in the recent past contained, HBCD. In fact, samples from the	(Zhu et al. 2017) was cited by the EPA.

	Wu et al., (2010) study were taken from a "natural pond in an e-waste recycling site." EPA might find the Zhu et al., (2017) study useful. • In terms of e-waste sites, a large percentage of the HBCD therein might be associated with High Impact Polystyrene (HIPS) (a dense plastic) or electronics solder/flux. Note that the Evaluation states (page 37) that a single U.S. company (Indium) employs HBCD in making solder flux. The material is exported "to their overseas facilities for the final mixing step and for sales to electronics manufacturers in China and the United States." The presence of HBCD within solder, textile/latex back-coating and HIPS matrices would result in different bioavailabilities and hence BAFs from what might be seen with polystyrene-associated HBCD. • He et al., (2013) also notes that tissue HBCD levels in the fish they sampled in China were ~10% those reported in a U.S.-based study by Chen et al., (2011) and in some European studies. The concentration differences might also impact estimates of accumulation and therefore the BAF estimates. The Committee considered the use of BAFs from these two China-based studies [BAFs from He et al., (2013) and Wu et al., (2010)] as not optimal, but unavoidable given that data for both ambient water and tissue in U.S. fish are lacking. (p. 105)	EPA agrees that characteristics of the matrix and other factors influence migration rates of HBCD from solid matrices and bioavailability. Little is known about the effect of the matrix on HBCD bioaccumulation factors. The uncertainties in assessing bioavailability of HBCD in matrices is discussed in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport. EPA acknowledges this comment.
SACC	**SACC COMMENTS:** • Rather than extrapolating bioaccumulation based on laboratory BCFs or field-derived BAFs alone from two Chinese studies, EPA should acquire more needed data by adding HBCD to the analyte list of major, existing monitoring programs; *e.g.*, its National Study of Chemical Residues in Lake Fish Tissue, National Rivers and Streams Assessment Fish Tissue Study, National Coastal Condition Assessment/Great Lakes Human Health Fish Tissue Study[9]. The Great Lakes Open Lakes Trend Monitoring Program10 may also be a source of data and opportunity. The possibility exists that archived tissue samples may be available from the above programs that could then be analyzed to determine contemporary biota burdens of HBCD. (p.	EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to make a reasoned analysis in light of the limited time available under the statute for completing the risk evaluation. As further noted in the response to the comments on the scope documents, EPA conducted extensive and varied data gathering activities including extensive and transparent searches of public databases and sources of scientific literature, government and industry sector or other reports, outreach meetings, searches of internal EPA databases, and more.

	110)	
SACC	**SACC COMMENTS:** • Discuss available data on HBCD concentrations in U.S. aquatic biota and compare to predicted model outputs. o Human consumption may include finfish, shellfish (such as mollusks or crustaceans), birds or mammals (*e.g.*, seals, whales or bears). The different life histories of these organisms may result in varying HBCD exposure and accumulation. Unfortunately, only a modest amount of data exists (although some have been published; *e.g.*, Chen et al., 2011) on HBCD concentrations in U.S. aquatic biota. Discussion of such data, in comparison to predicted model outputs would be useful. At a minimum, Section 2.3 should reference later sections (*e.g.*, Section 3.1) of the Evaluation where such data are more completely described. Additional North American data may be extracted from the "Binational Strategy for HBCD Risk Management"[7] and the "AMAP 2016: Chemicals of Emerging Arctic Concern"[8] reports (Artic Monitoring and Assessment Programme 2017). (p. 106)	Organism-specific life histories is a category of uncertainty in evaluating environmental risk and is addressed in Sections 3.1.7 and 4.3.1. For human consumption of aquatic biota, contributions to aggregate risk from fish consumption is evaluated for each of the general population from background exposure (Section 4.2.3), subsistence fishers based on increased fish consumption using various data sources for fish HBCD concentration (Section 4.2.3.2), and the highly exposed general population from COU-specific releases (Section 4.2.3.3).
SACC	**SACC COMMENTS:** • Consider issues identified for using laboratory studies to estimate BCF. o Bioconcentration factor (BCF) estimates from laboratory-based studies also have merit. Such laboratory studies allow for control of the mode, duration and composition (*e.g.*, diastereomers) of chemicals to which fish (or other organisms) are exposed. However, BCF calculation requires reliable and consistent water exposures and these may be difficult to achieve due to the hydrophobicity of HBCD. The Drottar and Krueger (2000) study cited in the Evaluation shows considerable variability in HBCD water concentrations over the course of the study, and measured water concentrations were about 53% of nominal/targeted values. It should be noted that this and several of the other studies cited (some externally peer-reviewed and published, others not) were conducted on the behalf of the	EPA acknowledges the data limitations and discusses the uncertainties in Section 2.1.3 Assumptions and Key Sources of Uncertainty for Fate and Transport

	flame-retardant industry. (pp. 106-107)	
SACC	**SACC COMMENTS:** • Consider issues identified for using BAF data for snakehead. o Wu et al., (2010) analyzed only six samples of snakehead fish from an e-waste impacted pond in southern China. Total HBCD concentrations (mean 187 ng/g lipid wt.) in Chinese snakehead were about 10-fold less than in riverine fish collected in the U.S. by Chen et al., (2011). Chinese mud carp concentrations (n=12; mean 868 ng/g lipid weight) reported in the Wu et al., (2010) study are actually higher than in the predatory snakehead. The mud carp's diet is dominated by consumption of soft sediments (Bowen et al., 2006). This may have led to their greater exposure to sediment associated HBCD. Prawn levels (395 ng/g lw, n=7) were also higher and more reproducible (lower coefficient of variation (CV)) than snakehead concentrations. Additionally, the relationship between concentrations and trophic level for total HBCD was not found to be statistically significant (p=0.12) by Wu et al., (2010). These data demonstrate that selection of BAF for the snakehead is neither protective of human health nor ecological receptors. (p. 107)	No studies of HBCD bioaccumulation in native U.S. fish had been found at the time of the risk evaluation. In the absence of those data, studies of HBCD levels in fish in China were used to derive BAF values. Those values were used with modeled or measured HBCD surface water concentrations to estimate fish tissue concentrations resulting from environmental releases of HBCD that may occur in the U.S. under relevant conditions of use. After the publication of the draft risk evaluation, a U.S. based study was identified measuring HBCD fish tissue concentrations from sites downstream from point source industrial releases and sites where industrial HBCD releases were not found. EPA used the highest concentrations in edible fish (carp and catfish) from the study to estimate HBCD exposures for subsistence fishers. These concentrations were about 10 times greater than those found in Chinese Northern Snakehead, Mud Carp and Suckermouth Catfish.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 3.4		
Degradation half-lives		
SACC	**SACC COMMENTS:** • Consider issues identified with estimating degradation half-lives. o The wide variations in abiotic and biotic characteristics of soils make derivation of HBCD half-lives a daunting problem. The best approach is to measure kinetic coefficients in several soil types (or other appropriate media). Modeling approaches require calibration with data from a range of soil types. More robust evaluation would also include testing at three or more environmentally relevant temperatures. To address this need, it would make sense to select soil types that are present in areas where manufacturing or end-product disposal is most likely. In the absence of such data, selection of the longest half-life	In response to the SACC comment, EPA further addressed uncertainty associated with biodegradation half -lives reported for HBCD by using Office of Pesticide Program guidance *Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation.* The Standard Operating Procedures were developed by scientists from U.S. EPA and the Pest Management Regulatory Agency of Health Canada in order to standardize approaches to characterize pesticide biodegradation rates and half-lives. It employs state of the science methodologies to derive data for use in pesticides assessments by NAFTA

	estimate (or 90th percentile of media specific half-lives) is one approach that would be cautionary and more protective. (p. 109)	partners. These procedures allow for the determination of the appropriate kinetics and associated half-lives for biodegradation studies. The guidance allows for a 3X factor to be used to account for uncertainty and variability where only 1 half-life value is available. In the final Risk Evaluation, the 3X factor was used with the longest reported half-life from Davis (2006) to give a half-life of 384 days. EPA believes the use of the longer half-life addresses concerns that an insufficiently conservative half-life was used. EPA conducted a sensitivity analysis using the range of reported half -lives including 384 days to determine the impact of half-life on modeled sediment concentrations. The results are presented in Section 2.13 Assumptions and Key Sources of Uncertainty for Fate and Transport Table 2-4 and further discussed in Section 4.1 Environmental Risk.
SACC	**SACC COMMENTS:** • Consider uncertainty issues identified with selecting HBCD degradation half-lives for modeling. o Models that utilize parameter values (specifically degradation half-lives) estimated from other models have significantly high uncertainties and often produce unreasonable results. It may be argued that taking the more conservative and defendable approach of using worst- (or near-worst) case measured half-lives provides greater certainty that false negatives are not driving the TSCA risk assessment process. The Committee noted that other halogenated chemicals such as PCBs and chlorinated insecticides that had been banned for decades are still circulating and detectable in the environment. However, there is a notable difference, in that the C-Cl bond is stronger than the C-Br bond. In summary, the Committee concluded that the HBCD half-lives chosen by EPA (see page 68: 2 to 6 months for aerobic soils and 11 days to 4 months for aerobic sediments derived from the Industry-sponsored Davis et al., studies (2005, 2006, 2009) are insufficiently conservative. (pp. 109-110)	In response to the SACC comment EPA further addressed uncertainty associated with biodegradation halflives reported for HBCD by using Office of Pesticide Program guidance *Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation.* The Standard Operating Procedures were developed by scientists from U.S. EPA and the Pest Management Regulatory Agency of Health Canada in order to standardize approaches to characterize pesticide biodegradation rates and half-lives. It employs state of the science methodologies to derive data for use in pesticides assessments by NAFTA partners These procedures allow for the determination of the appropriate kinetics and associated half-lives for biodegradation studies. The guidance allows for a 3X factor to be used to account for uncertainty and variability where only 1 half-life value is available. In the final Risk Evaluation, the 3X factor was used with the longest reported half-life from Davis (2006) to give a half-life of 384 days. EPA believes the use of the longer half-life addresses concerns that an insufficiently conservative half-life was

		used. EPA conducted a sensitivity analysis using the range of reported half-lives including 384 days to determine the impact of half-life on modeled sediment concentrations. The results are presented in Section 2.13 Assumptions and Key Sources of Uncertainty for Fate and Transport Table 2-4 and further discussed in Section 4.1 Environmental Risk.
#	**Summary of Public Comments for Specific Issues Related to Charge Question 3**	**EPA/OPPT Response**
General		
53	**PUBLIC COMMENTS:** • HBCD is ubiquitous in the Arctic, undergoes long-range atmospheric transport, bioaccumulates and the α-isomer biomagnifies, whereas the γ-isomer undergoes trophic dilution. o Arctic indigenous peoples are at risk of exposure to elevated levels of HBCD because of their reliance on fish, birds, and marine mammals as the basis for their traditional subsistence diets and should be evaluated as a potentially highly exposed subpopulation. o People of the north may be at higher risk to exposures through indoor air and dust because of greater periods of time spent indoors because of the long winters, low ventilation, and greater insulation of homes against the cold. Household dust contaminated with HBCD is an important exposure route. It is found in mother's breast milk; some breast milk studies show that levels of HBCD are increasing.	Risk estimation for subsistence fishers is discussed in Section 4.2.3.2. EPA assumed that these risk estimates are applicable to the majority of indigenous communities that rely on consumption of biota that may contain high levels of HBCD.
54	• EPA states that HBCD is expected to strongly sorb to soil particles, is not volatile, and would likely only escape to air through windblown soil particles. o EPA assumes that, due to HBCD's high soil adsorption coefficient, any potential migration of HBCD through the landfill to effluent would be slow. o This assumption does not account for the fact that foam board breaks up readily and can escape to air directly however, fugitive dust is not considered.	Due to the high variability associated with the release of HBCD to soil, a very high level of uncertainty would be associated with the assumptions that would have to be made to estimate resulting surface water concentrations and exposures. Qualitative discussion of this path of entry to the environment has been added. Dust emissions from landfills and its impact on general population would be driven by many unknown factors: amount of HBCD-containing materials per landfill, availability of HBCD containing materials at the surface, size of landfills and particle size. EPA did not quantify

		dust emissions from landfills in the final risk evaluation. EPA provides a qualitative discussion of HBCD in landfill leachate and potential for exposure in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle.

62	• When modeling HBCD concentrations in water and sediment, EPA "did not consider the potential impact of persistence and longer-term sinks [of HBCD] in lake and estuary environments."
	  o Habitats such as lakes and wetlands are known to accumulate higher concentrations of sediment contamination, as longer water residence times allow greater sorption of chemicals to suspended particulate matter, more time for sediment deposition, and prolonged contaminant persistence.
	  o Lack of consideration of these lentic habitats underestimates sediment concentrations near and downstream of point sources, and thus underestimates HBCD's risks.
		EPA reviewed available HBCD sediment monitoring data which it believes represents HBCD deposition over long -term use of HBCD. The monitoring data was considered in the risk evaluation.

62	• In its risk evaluation, EPA estimates HBCD's half-life in sediment to be 11-128 days.
	  o The studies cited, however, support a half-life that is considerably longer than the upper end of that range.
	  ▪ One study cited by EPA reported a 190-day HBCD half-life in sediment collected from Schuylkill River in Pennsylvania.
	  ▪ Another study, uncited by EPA, reported a half-life of 144-157 days.
	  ▪ Environment Canada and Health Canada have found the half-life of HBCD in sediment is "likely much longer than 365 days," based on both laboratory biodegradation testing and sediment core measurements.
		In response to the SACC comment, EPA further addressed uncertainty associated with biodegradation half -lives reported for HBCD by using Office of Pesticide Program guidance *Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation.* The Standard Operating Procedures were developed by scientists from USEPA and the Pest Management Regulatory Agency of Health Canada in order to standardize approaches to characterize pesticide biodegradation rates and half-lives. It employs state of the science methodologies to derive data for use in pesticides assessments by NAFTA partners These procedures allow for the determination of the appropriate kinetics and associated half-lives for biodegradation studies. The guidance allows for a 3X factor to be used to account for uncertainty and variability where only 1 half-life value is available. In the final Risk Evaluation, the 3X factor was used with the longest reported half-life from Davis (2006) to give a half-life of 384 days. EPA believes the use of the longer half-life addresses concerns that an insufficiently conservative half-life was used. EPA conducted a sensitivity analysis using the range of reported half- lives including 384 days to determine the impact of half- life on modeled sediment concentrations. The results are presented in Section 2.13 Assumptions and Key Sources of Uncertainty for Fate and Transport Table 2-4 and

62	• EPA's underestimate of HBCD's half-life results in lower predicted sediment concentrations and understates/ underestimates exposure to HBCD and risk.
	  o EPA should have used the highest half-life referenced in the studies it cites.
	  o Consistent with the more recent analyses conducted by the	

	Canadian government, EPA should also analyze the risks presented by HBCD using a sediment half-life of at least 365 days.	further discussed in Section 4.1 Environmental Risk.
62	**PUBLIC COMMENTS:** • When modeling HBCD concentrations in rivers, EPA relied on 7Q10 stream flows, or the lowest expected seven-day average stream flow over a ten-year period (measured in millions of liters per day). o This departs from EPA's own recommended approach for determining 7Q10 flows. o EPA used 50th percentile 7Q10 values, meaning that 50% of emitting facilities would be expected to discharge to a water body with 7Q10 flows equal to or lower than that selected by EPA. ▪ This is contrary to EPA's Sustainable Futures guidance, which recommends the use of 10th percentile 7Q10 values, or the rate at which only 10% of emitting facilities would be expected to discharge to water bodies with a lower or equal 7Q10 flow.	EPA acknowledges that we calculated both 10th percentile and 50th percentile in the draft risk evaluation, using the 50th percentile to inform the risk determination. In the final risk evaluation, EPA is using risk quotients based on the 10th percentile to inform the risk determination.
62	**PUBLIC COMMENTS:** • EPA underestimates HBCD's ecological risks and misinterprets its own calculations establishing that such risks are unreasonable. o EPA underestimates HBCD's environmental half-life and thus miscalculates the chemical's exposures and risks.	The environmental risk determination in the final draft risk evaluation has been updated to utilize the more robust and sensitive 10th percentile flow rate value for environmental exposure. A sensitivity analysis was also conducted to include additional HBCD half-lives and determine the impact on water column and sediment HBCD concentrations. EPA reviewed the input variables to the exposure models used for exposure estimates and selected values from studies of acceptable quality where uncertainties in measured values were minimized.
Species Selection		
62	**PUBLIC COMMENTS:** An inappropriate species selection to calculate human consumption of fish Species • EPA selected consumption and the bioaccumulation of HBCD in humans. o The risk evaluation uses the Northern Snakehead, an "upper trophic level species," as a surrogate species for the fish ingestion analysis. However, other investigated fish species	No studies of HBCD bioaccumulation in native US fish had been found at the time of the RE. In the absence of those data, studies of HBCD levels in fish in China were used to derive BAF values. Those values were used with modeled or measured HBCD surface water concentrations to estimate fish tissue concentrations resulting from environmental releases of HBCD that may occur in the US under relevant conditions of use.

62	considered by EPA had higher HBCD concentrations than the Northern Snakehead, such that EPA's choice of species underestimates risks to populations that consume those more contaminated fish. ○ Mud Carp and Suckermouth Catfish – both of which are bottom feeders that ingest HBCD-contaminated sediment – have average HBCD concentrations 1.9-4.6 times higher than those reported for the Northern Snakehead. ○ Carp and Catfish also provide more robust measures of fish concentrations because the cited studies sampled a larger number of individual fish for those species (n=10–12) than they did for the Northern Snakehead (n=6). ○ The Northern Snakehead is not a substantial part of the U.S. fish diet, whereas catfish species are. ○ EPA should have selected a more ecologically relevant and popular consumption species when calculating human exposure via fish ingestion. Such data was available in studies cited by EPA. • EPA selected Mink as a proxy for other mammal species. Selection of Harbor Seals as the receptor species would result in a better link to the aquatic and terrestrial food webs. There are monitoring studies of HBCD concentrations in Harbor Seals, which EPA should have considered in evaluating risks to mammals.	Subsequent to the publication of the draft RE, a US based study was identified measuring HBCD fish tissue concentrations from sites downstream from point source industrial releases and sites where industrial HBCD releases were not found. EPA used the highest concentrations in edible fish (Common Carp) from the study to estimate HBCD exposures for subsistence fishers. These concentrations were about 10X greater than those found in Chinese Northern Snakehead, Mud Carp and Suckermouth Catfish (Chen et al. 2011). Mink was chosen as the representative terrestrial predator of aquatic prey (*i.e.*, fish), because HBCD trophic transfer is not limited to aquatic ecosystems; Mink diet is characterized in the U.S. EPA Wildlife Exposure Factors Handbook, and therefore used to assess how 100% fish diet may result in HBCD uptake by a terrestrial organism that inhabits and consumes prey from aquatic ecosystems. The use of monitoring studies to characterize risk to Harbor Seals or other organisms that primarily consume fish and inhabit both aquatic and terrestrial ecosystems would still only provide exposure estimates; hazard and risk will still be difficult to characterize.

Environmental Release – Public and Peer Review		
Charge Question 4.1: Please comment on the methods and approaches used for environmental release estimation. **Charge Question 4.2:** Please provide any specific suggestions or recommendations for alternative data sources, or estimation methods that could be considered by the Agency for conducting environment release assessment		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 4**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 4		
Additional releases to consider		
SACC	**SACC COMMENTS:** • Consider disposal of polystyrene and other plastic components impregnated with HBCD in the analysis of environmental exposure routes and as Solid Waste Disposal activity/uses in the conceptual model for environmental releases. (p. 114) ○ If there is continued use of HBCD or presence in building materials, there is significant uncertainty in the movement and breakdown of disposed materials from soils and in particular from landfills into air and waterways (particularly oceans). (p. 113) • Without data, emissions scenario documents (ESDs) or generic scenarios (GSs) for plastics (see Section 2.2.1) cannot be used as surrogates. Use of ESDs or GSs in lieu of data represents another source of uncertainty that should be discussed, particularly for the demolition and disposal of polystyrene derived foam. (p. 114)	As indicated in the HBCD Risk Evaluation, EPA did not estimate releases from demolition based on emissions scenario documents (ESDs) or generic scenarios (GSs). Using particle generation factors reported in the EU RAR (European Commission, 2008), EPA calculated the release rate of particles containing HBCD that are generated during demolition and assessed the media of release of these particles to include fugitive air, surface water, and/or POTW. EPA also estimated the amount of HBCD in demolition debris that is sent to construction and demolition landfills and municipal incinerators. EPA provided discussion of the uncertainties in estimating the release of HBCD from landfills in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle. EPA discussed the release of HBCD to the environment, including the marine environment, from microplastics in Section 2.1.3 of the HBCD Risk Evaluation.
SACC	**SACC COMMENTS:** • Consider leachate from landfills a source of input to the environment and as Liquid Waste uses in the conceptual model for environmental releas**es.** (p. 114) ○ If there is continued use of HBCD or presence in building materials, there is significant uncertainty in the movement and breakdown of disposed materials from soils and in particular from landfills into air and waterways (particularly	EPA has considered the concentrations of HBCD reported in landfill leachate particulates from the Netherlands cited in the EU 2008 report. The values cited by the commenter were measured concentrations in leachate from two of nine landfills studied (de Boer et al., 2002). The range of concentrations in landfill leachate particulates from the seven other landfills sampled were approximately two orders of magnitude lower than those cited by the

	oceans). (p. 113) • After heavily relying on the EU 2008 report for some data, much of the remaining data and estimates are omitted or ignored. For example, ignored are measured releases reported in the data of 22 mg/g (dry weight) and 67 mg/g (dry weight) for solids in landfill leachate. (p. 114) • Consider additional HBCD releases from other uses and disposal ○ The magnitude and scope of releases assumed in the Evaluation are too constrained. After heavily relying on the EU 2008 report for some data, much of the remaining data and estimates are omitted or ignored. For example, ignored are measured releases reported in the data of 22 mg/g (dry weight) and 67 mg/g (dry weight) for solids in landfill leachate. The Committee considers that a scientifically defensible evaluation requires considerations of these releases and all other types of releases from materials actively in commerce or actively being disposed that contain HBCDs. (p. 114)	commenter. EPA discusses studies demonstrating the presence of HBCD in landfill leachate and provides rationale for why the leachate exposure pathway was not quantitively assessed in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle.
Clarifications		
SACC	**SACC COMMENTS:** • Provide information to clarify statement about small processors. ○ The Committee expressed concerns that there is no evidence to back up the statement on page 24 that "It is possible, however, that smaller processors may still be using the chemical, although evidence of this has not been found and EPA has not received information that this is occurring." (p. 114)	Section 1.2.5.2 of the Risk Evaluation provides the rationale for including the use of EPS and XPS foam insulation in the evaluation. While EPA could not find direct evidence that EPS and XPS processors are currently using HBCD, the rationale for including this use in the Risk Evaluation is as follows. There is a potential for import of HBCD for use in the manufacture of EPS and XPS foam insulation. Taking into account the high percentage of HBCD production volume dedicated to these two uses in previous years, and the fact that small HBCD companies could import low volumes of the chemical that would not be reported to CDR leaves open the possibility that EPS and XPS manufacturers that are not members of the EPS-Industry Alliance and the Extruded Polystyrene Foam Insulation (XPSA) may currently be using imported HBCD resins in their processes. EPA included the processing and use of HBCD in XPS and EPS insulation and import of HBCD resin in

		the risk evaluation.
SACC	**SACC COMMENTS:** • Clarify relationship between "condition of use" and current risks. o According to the phase-out information provided in the Evaluation, it is unclear how "condition of use" and current risks are related. Clearly, when HBCD is used or present during use of materials containing HBCD, there is apparent risk to ecological receptors. Consequently, it is unclear whether this constitutes a cleanup issue rather than a "use" issue. (p. 113)	TSCA requires EPA to evaluate the risks of chemical substances under their conditions of use. (TSCA Section 6(a). The phrase "conditions of use" means "the circumstances under which a chemical substance is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used or disposed of." (TSCA Section 3(b)(4)) The use of HBCD and HBCD-containing materials are conditions of use, therefore EPA evaluated the risks to human health and the environment from exposure to HBCD during its use. Cleanup of contaminated media is outside the scope of the risk evaluation.
SACC	**SACC COMMENTS:** • Clarify impact of apparent omission of releases from many known sources of HBCD. o Releases from many known sources of HBCD seem to be missing in the Evaluation. This omission is expected to lower exposure estimates and thus underestimate risk. If there is continued use of HBCD or presence in building materials, there is significant uncertainty in the movement and breakdown of disposed materials from soils and in particular from landfills into air and waterways (particularly oceans). Using a multimedia fugacity model, Tomko and McDonald (2013) showed that leachate from landfill and recycling facilities in Canada clearly moved into environmental media. (p. 113)	EPA discusses studies demonstrating the presence of HBCD in landfill leachate and provides rationale for why the leachate exposure pathway was not quantitatively assessed in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle.
SACC	**SACC COMMENTS:** • Provide support for confidence assumption for estimates in Table 2-7. o On page 80, the EPA states that they have medium to high confidence in the release estimates provided in Table 2-7; however, differences between disposal of transport bags and	Information that is relevant to EPA's approach to the determination of confidence in the risk evaluation results pertaining to occupational exposure is given in Appendix E.7 of the HBCD Risk Evaluation, which is a description of EPA's data integration approach and the factors considered in determining levels of confidence. The confidence rating of the Repacking of Import Containers

	dust releases are exactly one order of magnitude. The Agency needs to support this assumption that would justify its medium to high level of confidence. This could be accomplished with a footnote to the table. (p. 114)	was revised from medium-high to medium. The confidence ratings considered: quality of the data, representativeness of the data for the exposure scenario, and uncertainties in the assessment. The data quality score for the parameters used in the referenced scenario is medium. The parameters used were based on emission factors and release information for use of flame retardants in the plastic industry. EPA considers such potential release activities as dust emitted during unloading and cleaning transport containers to be similar to the repackaging of HBCD. Sources of uncertainty are potential differences in process volumes, transport containers, and waste management practices between sites. EPA also acknowledges additional uncertainty with predicted release days. EPA accounted for this uncertainty by assessing a range of emission factors and release days to estimate a potential range of daily releases from the repackaging of HBCD.
Obtain Additional Data		
SACC	**SACC COMMENTS:** • Obtain data from pre-Stockholm convention users. o The Committee recommended that EPA actively seek use information from all potential pre-Stockholm convention users or assume that at least a sizeable fraction of pre-Stockholm convention users is importing 25 to 100,000 pounds per year. Perhaps a Significant New Use Regulation (SNUR) covering all uses would help fill this information gap. (p. 114)	The Risk Evaluation's scope includes uses that are known, intended, or reasonably foreseen to occur within the boundaries of the United States. EPA acknowledges the suggestion that EPA promulgate a Significant New Use Rule for HBCD.
SACC	**SACC COMMENTS:** • Obtain data about imports of insulation foam. o Data on imports of insulation foam should be obtained and incorporated in use estimates. (p. 114)	Data on the volume of HBCD containing insulation imported into the United States are not reasonably available. Import of a chemical substance as part of an article is not subject to CDR reporting (40 CFR 711.10(b)).
#	**Summary of Public Comments for Specific Issues Related to Charge Question 4**	**EPA/OPPT Response**

Disposal of products containing solder paste		
58	**PUBLIC COMMENTS:** • Disposal of products containing solder is not included in the risk evaluation; under TSCA, product disposal must be considered.	As described in Section 2.4.1.13 of the final risk evaluation, HBCD is expected to degrade at the soldering temperature (200-300 °C), and hence EPA assumes that HBCD degrades during the use of the solder paste and products do not contain HBCD.
Landfill release		
62, 58, 54	**PUBLIC COMMENTS:** • Environmental releases from landfills were inadequately addressed; the assumptions made regarding disposal site management and protective design should be clearly stated. o Landfill releases are only qualitatively discussed; a quantitative evaluation is needed. ▪ EPA states that over 99% of landfill releases are expected to be from insulation and recognizes that there is potential for HBCD released from landfills to migrate to the nearby environment. ▪ There are also no federal standards for management controls that might mitigate this release (*e.g.,* coverings, liners, and treatment) and C & D landfills, where the majority of waste containing HBCD is disposed, often, and in many states typically, have no such controls. ▪ Many communities in rural areas live in proximity to C & D landfills and are potentially exposed to landfill releases. o Fugitive dust at landfills and transfer stations was not considered. o HBCD is present in landfill leachate, mostly in the particulate phase, and EPA must consider landfill releases of HBCD to the environment in the final risk evaluation. o Environmental releases from RCRA Subtitle D landfills for the State of Alaska were not considered. Many communities in Alaska only have access to unlined landfills, with no leachate treatment, and infrequent cover; these landfills are fully accessible to the public. ▪ Alaska is one of numerous states that allow C & D landfills to be unlined.	Dust emissions from landfills and its impact on general population would be driven by many unknown factors: including, but not limited to the amount of HBCD-containing materials at the landfill, availability of HBCD containing materials at the surface, and size of landfills. The largest source of HBCD waste to landfills is expected from the demolition of buildings, EPA estimated this amount per year in Section 2.2.10. EPA did not calculate an average amount of HBCD waste per landfill as EPA expects the rates of demolition will vary between regions with certain areas having high rates of buildings renovation/demolition and the distribution of HBCD waste disposed between landfills would therefore be expected to vary. EPA provides a qualitative discussion of HBCD in landfill leachate and potential for exposure in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle. EPA agrees that the references cited suggest pathways exist from industrial sources of HBCD emissions to soil and water. The studies indicate higher HBCD concentrations in soil and water in samples collected in areas with industrial impact. Brandsma noted the possible influence of textile and brominated flame retardant manufacturing and Tang noted the possible influence of e-waste dumping sites and industrial areas. However, neither study provided quantitative information on releases or environmental concentrations resulting from HBCD COUs that could be used in the final risk evaluation.

	▪ Exposures and risks from landfills should be evaluated. o Landfills and transfer stations should be considered a facility and HBCD releases from them should be modeled, since environmental release data used for facilities include disposal site near-release. o EPA claims that "[i]f the annual releases were divided by the number of active landfills in the US and the average size of a landfill in the U.S., and … this mass [was divided] into the top … layer of soil in a landfill [,] this concentration would approximate central tendency estimates from [HBCD] soil monitoring data." ▪ No evidence was provided indicating that HBCD – containing insulation would be equally distributed among all landfills, or evenly within a landfill. ▪ If uneven, or disproportionate shares of the waste are going to unlined landfills, some communities could be at greater risk of exposure than the general population and should be evaluated as a highly exposed subpopulation. o EPA states "In summary, under some conditions it is possible that landfills represent a potential source of exposure to the nearby environment," but does not assess the associated risks. ▪ EPA should provide an explanation for this decision. ▪ Without further analysis, EPA cannot make a finding of no unreasonable risk.	
54	• Brandsma (2015) and Tang et al., (2014b) found release of HBCD from disposal sites in highly organic matrix via leachate particulate-phase migration in the water; both studies showed elevated to extremely elevated off-site HBCD particulate-phase concentrations from disposal sites. ▪ Although the above studies were cited, it is not clear they were used in the surface water evaluation. These studies provide that support that a pathway of release of HBCD from materials or landfills exists, including direct drainage to surface water.	

62	**PUBLIC COMMENTS:** • EPA acknowledges "there is potential for HBCD released to landfills to migrate to the nearby environment, but states that "controls such as coverings, liners, and treatment may partially or fully mitigate this." o EPA must support the assumption that HBCD, which is not listed as a hazardous waste under the Resource Recovery and Control Act ("RCRA") and historically has not been sent to hazardous waste landfills, is likely to be disposed in landfills with these controls. o EPA does not evaluate the effectiveness of such controls – even if present – in preventing releases of HBCD. ▪ International studies have concluded that "the leakage of landfill leachate could significantly contribute to the [HBCD] contamination of both surface and groundwater sources." ▪ EPA should evaluate the risks posed by HBCD landfill leachate or present any determination concerning whether such risks are unreasonable.	EPA has qualitatively assessed the potential for landfilled HBCD to migrate and reach receptors as described in Section 2.4.5.2. Insufficient information is reasonably available to quantify exposure from landfill leachate.
Clarity About Data Use		
45 31, 54, 45	**PUBLIC COMMENTS:** • EPA explains its general approach to assessing releases to the environment as utilizing production volumes, emission factors, and number of days of release per year, to inform its assessment. But EPA also states that sometimes Toxics Release Inventory (TRI) data are used instead of production volume and emissions. o EPA should clarify why TRI data were used in some cases while not in others. o Since TRI data represent estimated releases to the environment, not measured releases, when EPA relies on TRI it should explain why this substitution was necessary. o It is not clear if TRI data are appropriate and fit-for-purpose in these cases.	As presented in the *Systematic Review Supplemental File: Data Quality Evaluation for Environmental Releases and Occupational Exposure Common Sources*, EPA evaluated information from TRI reporting to be of medium quality. In the HBCD risk evaluation, when available for the exposure scenario, waste management releases reported to 2017 TRI were used in estimating potential releases, along with other reasonably available data sources. For most release scenarios, information from TRI reporting was not reasonably available. EPA describes the data integration approach and factors considered in Section 2.2.1 and in Appendix E.7 of the HBCD Risk Evaluation. Generally, EPA considers measured and monitoring data on releases over modeled estimates. For the final Risk Evaluation, EPA provided

54 53	• At a minimum, EPA should include a flow chart describing how EPA utilizes both monitoring data and modelling data to inform a tiered approach to assessment. • EPA cited a recent study showing that HBCD migration from materials into effluent can occur and is influenced by experimental conditions, mimicking real-world conditions (Stubbings and Harrad, 2014). • The Arctic Monitoring and Assessment Program (AMAP) reports have data on the ubiquitous presence of HBCD in northern and Arctic environments, including air, sediments, freshwater and marine biota. These data should be reviewed.	release estimates based on available data that were of acceptable quality based on the criteria in *Application of Systematic Review in TSCA Risk Evaluations*. (Stubbings and Harrad 2019) and HBCD in landfill leachate is discussed in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle. Upon further investigation, the AMAP report had no supporting information based on a search for HBCD.
Other Potential Sources of HBCD Release into the Environment		
53, 62, 55	**PUBLIC COMMENTS:** • Consumer products (polystyrene products in food packaging, appliances, insulation, buoys used in aquaculture facilities). HBCD can be released from consumer products during production, use, and disposal. • Polystyrene marine plastic debris.	For direct consumer exposure, EPA assessed children's mouthing of articles, insulation in homes, and car consumer use scenarios. Uncertainties associated with release of HBCD from products are discussed in Section 2.1.3. Some of the products noted in the comment were not confirmed as having HBCD in them in the United States (*e.g.*, appliances, buoys). For those covered under EPA's authority, EPA considers it unlikely that HBCD will be manufactured for use in or incorporated into any product or article for which manufacture with HBCD has been discontinued, because manufacturing, import, and use of HBCD has dramatically declined and is phasing out worldwide, including in the United States. No data were extracted that deal with marine plastic debris except for those dealing with aquatic species receptor (Jang 2016).
53, 62, 55	**PUBLIC COMMENTS:** • Transportation of disposal and waste to the Arctic from global distillation.	EPA agrees that HBCD, like other persistent semi-volatile chemicals, may reach the Arctic by global distillation. The long- range transport potential of HBCD is discussed in the Fate section. This source is reflected in environmental

		monitoring data cited in the final Risk Evaluation.

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53, 62, 55
	PUBLIC COMMENTS:
	• Open burning and dump sites containing demolition and construction debris.
	• Incinerators
	  ○ EPA does not provide data on the expected HBCD emissions from incinerators or evaluate risks to downwind communities.
	  ○ EPA does not state what chemicals are released as a result of that thermal degradation or consider their effects on the workers who will be inhaling them.
		The TSCA risk evaluations cover current and ongoing disposal of HBCD, an assessment of 'legacy disposal' is not within the scope of the risk evaluation. EPA notes that the open dumping of solid waste including construction and demolition waste is federally prohibited by RCRA subtitle D. EPA also notes that the open burning of construction and demolition debris may be regulated at the state level. In the PESS discussion in Section 4.4.1, EPA has added open burning as an example of "other activities" which were not further characterized in this Risk Evaluation.
		
		In the HBCD risk evaluation, EPA estimated the daily and annual HBCD waste per facility for each exposure scenario and evaluated its potential to be released, disposed, treated (*e.g.*, treated via incineration), or discharged. EPA utilized the Integrated Indoor Outdoor Air Calculator (IIOAC) to calculate air concentrations for both fugitive emissions and emissions from incinerators. This is explained in Sections 2.2 through 2.3.

Occupational Exposure – Public and Peer Review Comments		
Charge Question 5.1: Please comment on the estimation methods and approaches used for occupational exposure assessment. **Charge Question 5.2:** Please provide any specific suggestions or recommendations for alternative data, or estimation methods that could be considered by the Agency for conducting occupational exposure assessment.		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 5**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 5		
Clarifications		
SACC	**SACC COMMENTS:** • Provide data or other justification in support of the assumption that any inhaled particulate would either be absorbed through the lungs or swallowed and subsequently absorbed in the GI tract. (p. 119). • The Committee also agreed that, given the stated particle size of HBCD dust (excluding the finest grade, which is not used in the U.S.), the assumption that particles will deposit in the upper and ciliated airways and then be ingested is reasonable; very few of these particles would be expected to reach the lower respiratory tract. However, the Committee considers the assumption stated on page 178 that "…all inhaled particles that are not respirable are deposited in the upper respiratory tract" and "all inhaled particles are either absorbed in the lung or in the intestine after ingestion" and on page 352, "It is assumed that any inhaled particulate would either be absorbed through the lungs or swallowed and subsequently absorbed in the GI tract" not to be supported by the data (discussion not found in Section 4.2.1 as indicated on page 178, but in Section 2.4.2.5). There is no supporting information as to why particles of this composition and size can be absorbed into the lung either passively or actively. (pp. 116-117) • Address uncertainty associated with assumptions about dust from construction/demolition debris.	EPA deleted all mention of this assumption in Section 2.4.1, Occupational Exposures because this assumption is unrelated to the topic of Section 2.4.1 and is instead related to the topics of Sections 3.2.2 and 4.2.1. These two sections include a discussion that addresses the SACC comment. Also, EPA made other changes to Sections 2.4.1 and 4.2.1 in response to the peer review comment as further discussed below. EPA revised Section 2.4.1 to state the following: the worker monitoring data comprise concentrations of HBCD in inhalable and respirable dust; EPA assessed worker exposure to inhalable dust only and EPA's rationale for doing so is discussed in Section 4.2.1. EPA also made the following changes to Section 2.4.1 which are related to the peer review comment: a) clarification of the physical form of the HBCD that workers are potentially exposed to in the case of worker inhalation monitoring data pertaining to the handling or processing of XPS masterbatch and XPS foam; EPA did so by stating that workers are potentially exposed to HBCD contained in dust that is composed of airborne particles of XPS foam or XPS masterbatch; b) deletion of all statements in Section 2.4.1,

	• EPA made several assumptions regarding "recycle dust" associated with HBCD-containing construction demolition debris. Many of these assumptions were viewed as speculative by Committee members, given no area or personal breathing zone or particle size(s) data on these dusts are available. As a result, there is a great degree of uncertainty about the disposition of the inhaled material within the airways and lungs and how efficiently it is transferred to systemic targets. (p. 154)	Occupational Exposures, that the HBCD contained in XPS or EPS foam particles or in XPS masterbatch particles may not be fully absorbed in the human body in the case of worker exposure to HBCD that is in these physical forms; c) mention of potential exposure to HBCD nanoparticles as a result of cutting of XPS/EPS foam by hot wire and characterization of the material emitted from hot wire cutting. A short discussion was previously included at the end Section 4.2.1 and EPA has added language to clarify that ingestion of these particles is most likely, however this assumption does not affect exposure/risk estimates: "For inhalation exposure, EPA considered the quantification of incidental ingestion of particulates that would result from exposure to HBCD dust in occupational, environmental, or residential settings. It is assumed that any inhaled particulate would either be absorbed through the lungs or swallowed and subsequently absorbed in the GI tract. Based on available toxicokinetic data, EPA conservatively assumes 100% absorption through the lungs and GI tract, although the majority of HBCD particles are likely to deposit in the upper respiratory tract and be ingested. EPA is not estimating risks for any respiratory-specific hazards associated with HBCD exposure. Since all HBCD hazards evaluated through dose-response analysis involve systemic toxicity, it is irrelevant for the purposes of this assessment whether HBCD is absorbed through the lungs or GI tract. Therefore, EPA used total inhalation exposure values (as opposed to only respirable) for risk estimation."
SACC	**SACC COMMENTS:** • Describe the potential for underestimation of U.S. workers' exposures when basing occupational exposures on the European PNOR TWA of	EPA revised Section 2.4.1.14, Assumptions and Key Sources of Uncertainties for Occupational Exposures, and discussed European occupational exposure limits

	10mg/m^3, which is lower than the U.S. OSHA PEL of 15mg/m^3. Incorporate this discussion into the analysis of uncertainties and confidence around these estimates. (p. 119-120) • The Committee agrees that using surrogate European data for packaging is acceptably justified and EPA recognizes most of the limitations of doing so. However, the Committee notes that the European occupational standard for the equivalent of the Particulates not Otherwise Regulated (PNOR) 8h-TWA is 10mg/m^3, lower than the U.S. OSHA PEL of 15mg/m^3 (although similar to the California (CAL)-OSHA PEL of 10mg/m^3). Consequently, occupational exposures in Europe may be controlled to meet a lower standard than in the U.S., resulting in potential underestimation of U.S. workers' exposures when basing these estimates on European occupational exposure data. The Committee recommended that EPA describe this potential source of bias in its exposure estimates and incorporate this into the analysis of uncertainties and confidence around these estimates. (p. 119)	in this section. Specifically, EPA stated there is uncertainty whether the monitoring data for workers in Europe are representative of the exposure levels for workers in the U.S. There is additional uncertainty in whether the types of engineering controls used in Europe are similar to those used in the U.S. since the OSHA PEL in the U.S. is different than that in Europe for Particulates Not Otherwise Regulated (PNOR; 15 mg/m3 versus 10 mg/m3, respectively).
SACC	**SACC COMMENTS:** • Justify why sometimes the same qualitative level of confidence is applied to exposure estimates that are derived from monitoring data as to estimates derived from surrogate data or model results. (p. 120) • The Committee agrees that EPA's approach of providing a qualitative level of confidence for the overall estimates of exposures for each Condition of Use (COU) is appropriate and should be adopted for other TSCA Risk Evaluations (REs). However, it is not clear why sometimes the same qualitative level of confidence is applied to estimates that do not appear to have the same level of reliability. For example, the same level of confidence is applied to estimates derived from actual monitoring data and from surrogate data without any clarification. (p. 119)	EPA's approach on deriving confidence rating in the risk evaluation results pertaining to occupational exposure is given in two documents about systematic review and in the final HBCD Risk Evaluation. These two documents about systematic review are the following: (1) *Application of Systematic Review in TSCA Risk Evaluations*, which contains the descriptions of data quality ratings, and (2) Appendix E.7 of the HBCD Risk Evaluation, which contains a description of EPA's data integration approach and the general factors considered in determining levels of confidence. The final HBCD Risk Evaluation contains information about EPA's approach on deriving confidence levels pertaining to the various occupational exposure scenarios in the following sections: 2.4.1.2 to 2.4.1.7, 2.4.1.9 to 2.4.1.12 and 2.4.1.14. EPA then revised the assessed confidence levels in the case of several occupational exposure

		scenarios consistent with the approaches referred to above. Specifically, EPA revised the confidence level pertaining to four exposure scenarios from a confidence of medium to high confidence to a confidence level of medium. These exposure scenarios are the Compounding of Polystyrene Resin to Produce XPS Masterbatch, the Processing of HBCD to Produce XPS using XPS Masterbatch, the Processing of HBCD to Produce XPS Foam using HBCD Powder and the Recycling of EPS Foam and Reuse of XPS foam. Also, EPA revised the confidence level pertaining to three exposure scenarios from a confidence of medium to a confidence level of low to medium. These exposure scenarios are the Processing of HBCD to Produce EPS Foam Using Imported EPS Resin Beads, the Processing of HBCD to Produce SIPs and Automobile Replacement Parts from XPS/EPS Foam, the Installation of XPS/EPS Foam Insulation in Residential, Public and Commercial Buildings, and Other Structures. The confidence ratings pertaining to the occupational exposure scenarios are listed in Table 2-71 in Section 2.4.1.1 of the final Risk Evaluation. As discussed in Table 2-70 of the final Risk Evaluation, EPA assessed all occupational exposure scenario based on HBCD worker monitoring data with one exception. This exception is the scenario of Demolition and Disposal of XPS/EPS Foam Insulation Products in Residential, Public and Commercial Buildings, and Other Structures. EPA assessed this scenario based on the Occupational Safety and Health Administration (OSHA) permissible exposure limit (PEL) for particulates not otherwise regulated (PNOR) and the confidence rating pertaining to this scenario is low to medium as mentioned above. The confidence rating pertaining to other occupational exposure scenarios is also low to medium as specified above; the reason for this confidence rating is that EPA assessed all of these

		scenarios based on the same HBCD worker monitoring data and there are deficiencies in this data as discussed in the sections of the final Risk Evaluation that pertain to the relevant exposure scenarios.
SACC	**SACC COMMENTS:** • Document the level of effort used to acquire the original and complete data from the European studies. (p. 120) • The Committee questions whether any attempt was made by EPA to obtain the original and complete data from the European studies. EPA's treatment of the summary data is satisfactory, but it is not clear whether the individual point data can be judged as not reasonably available without evidence that there was an attempt to obtain it from the authors and/or sponsors of the study. (p. 119) • Similarly, it is not clear why EPA could not attempt to contact the authors or organization funding the European studies to get information about the treatment of lower limits of detection (LOD) values. (p. 119)	EPA unsuccessfully sought all primary data sources which are held by foreign entities. The primary data source containing most of the occupational exposure monitoring data that EPA mentions in the HBCD Risk Evaluation is the following report: Searl A and Robertson A. 2005. Workplace exposure to hexabromocyclododecane (HBCD) in the European Union. Report for the European Brominated Flame Retardant Industry Panel. IOM Consulting, Edinburgh. EPA requested this report from the following organizations: the Swedish Chemical Agency, the rapporteur of the EU's risk assessment on HBCD, IOM Consulting, the authors of the report, and the European Brominated Flame Retardant Industry Panel, the commissioner of the report. Both the Swedish Chemical Agency and the IOM Consulting indicated that they could not provide the original data in this report. EPA did not receive a response from the European Brominated Flame Retardant Industry Panel.
ONU Exposures		
SACC	**SACC COMMENTS:** • Recognize that ONU's exposures in certain work environments could be similar to those experienced by the workers and discuss how this potentially changes ONU exposure estimates. (p. 119) • The Committee agrees that occupational non-users (ONUs) would likely have lower exposures than workers. However, this may not be the case	EPA agrees that the HBCD potential exposure levels of construction and demolition ONUs may not be lower than HBCD potential exposure levels of construction and demolition workers. Accordingly, EPA revised Section 2.4.1.1, Occupational Exposures Approach and Methodology and Section 2.4.1.14, Assumptions and key Sources of Uncertainties for Occupational Exposures, to discuss this uncertainty.

	for some types of work where workers may be performing different tasks in close proximity to primary operations, with only some of them directly in contact with HBCD-containing materials. An example would be installation or removal of building materials in enclosed construction spaces where different categories of workers may be performing a variety of tasks, but all are exposed to the dust generated by some workers cutting insulating foam panels. At a minimum, EPA should recognize that ONU's exposures could be similar to those experienced by the workers and provide examples of work sites and jobs where this may be the case. (p. 117)	
Dermal Exposures		
SACC	**SACC COMMENTS:** • Compute dermal uptake using the flux-based approach and compare results to estimates obtained via the fixed fractional absorption approach. (p. 119) • One Committee member provided extensive discussion on the approach to estimating dermal absorption. Use of fixed fractional absorption to predict dermal uptake is inferior to modeling using a flux-based approach. Fractional absorption depends on loading, so the fixed-fraction-absorbed approach can easily lead to overestimation of absorbed dose at high potential dose, and underestimation at low potential dose. (p. 117)	EPA refers the commenter to Appendix L, Dermal Absorption Estimate Method Comparison. When using very conservative assumptions of maximum flux, solvent, and time allowed for absorption, the upper-bound dermal absorption estimates are consistent between the fraction absorbed and permeability methods (based on data from Abdallah et al., 2015).

SACC	**SACC COMMENTS:**
	• Consider divergent viewpoints from reviewers about EPA's assumptions on dermal absorption of HBCD.
	• The Committee did not reach consensus on EPA's assumptions on the dermal absorption of HBCD from beads or foam particles deposited on the skin. [NOTE: bullets were added below to distinguish viewpoints; not from original text]
	  • Some Committee members agreed with EPA's approach.
	  • One reviewer felt that the assumption that HBCD in beads or in
		EPA assumes HBCD in beads or in foam are not available for contact with skin and thus absorption is based on judgment that the HBCD in beads or in foam will be contained within the matrix. EPA did not identify any relevant references through its systematic review process. EPA includes this as an uncertainty.

	foam particles would not be available for contact with skin (and thus absorption, because it is captured within the matrix) should be supported by data, such as HBCD migration from beads or foam into simulated perspiration. In the case of beads, some HBCD could be present on the surface if the beads are not encapsulated. • Another reviewer felt that because bromine atoms are very dense, and brominated compounds tend to have high specific gravities, quantitative structure activity relationship (QSAR) techniques that use molecular weight as a surrogate for molecular size tend to overestimate the size of brominated compounds. HBCD, with a molecular weight of 646, would be about the same size molecule as a hydrocarbon with a molecular weight of under 300. HBCD therefore may be small enough to permeate skin. (p. 117)	
PPE		
SACC	**SACC COMMENTS:** • Present scenarios and base final risk decisions on the assumption of limited likelihood that respiratory protection will be adopted without specific occupational exposure guidelines for HBCD. (p. 119) • The Committee agrees that mitigation approaches are well summarized. However, many members of the Committee believed EPA should place more emphasis on the limited likelihood that respiratory protection will be adopted without specific occupational exposure guidelines for HBCD (one reviewer stated that the general dust exposure limits are appropriate). (p. 118) • Dust exposures in the construction trades (especially residential construction) continue to represent an occupational health concern because of the many small-to-medium size operators and the use of temporary (and, not infrequently, undocumented) workers. Workers in these small-to-medium enterprises may not be likely to adopt personal protective equipment (PPE) controls, so EPA's characterization of	While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. For the purposes of determining whether a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties. Based on SACC comments, EPA in its revisions is assuming that workers in the construction and demolition OES are unlikely to wear PPE. Risk conclusions will therefore be based on risk estimates without PPE for those OES.

	reasonable risk relying on use of PPE is not sufficiently supported by the practical realities of many workplaces. (p. 118)	
SACC	**SACC COMMENTS:** • Use human skin results from Abdallah et al., paper instead of cell culture results. ○ The human skin results from Abdallah et al., should be preferred over the cell culture results based on historical experience with the latter approach (although in this case the cell culture results are not very different). (p. 118)	As mentioned by the panel, the results are quite similar, and EPA acknowledges that its assumptions are an upper-bound estimate. Therefore, EPA used the highest values in order to be health protective while acknowledging that the dermal exposure estimates are likely to overestimate risk.
SACC	**SACC COMMENTS:** • Consider information about skin depot reported in Roper et al., paper. ○ Roper et al., note the formation of a skin depot that they interpret as evidence of poor permeability of the stratum corneum. What it may instead demonstrate is that the viable epidermis should control permeation to the blood stream for a lipophile like HBCD, and that a reservoir builds up above the viable epidermis. This reservoir would be available to support maximum flux through the viable epidermis beyond the workday and making the exposure duration 24 h. The depot reported by Roper et al., is so large that it implies flux into the stratum corneum that is disproportionate to flux into the receptor fluid. This observation merits further consideration (*i.e.*, might reflect an experimental anomaly). (p. 118)	EPA agrees with this discussion. The assumption of a 24hr exposure duration has been incorporated into the calculations comparing flux and fractional absorption in Appendix L.
Other Panel Recommendations		
SACC	**SACC COMMENTS:** • Consider potential effects of larger effective surface area of potential contact with lung lining fluid for HBCD-containing foam particles. • Additionally, EPA should consider that HBCD-containing foam particles are porous and hence have a larger effective surface of potential contact with lung lining fluid than the solid HBCD beads of similar size. Although leaching of HBCD into lung fluid is likely minimal due to HBCD's physicochemical properties, the large surface area of potential	EPA conservatively assumes that the entirety of inhaled HBCD (based on estimated exposure to inhalable particles < 100 micron) will be absorbed, either through the lungs or through the gut after swallowing. Therefore, EPA is already accounting for plausible leaching of HBCD out of foam.

	contact could result in more than minimal total leaching of HBCD from the foam particles into the lung lining fluid and partial absorption into the systemic circulation. These concerns are also relevant for Question 11. (p. 117)	
SACC	**SACC COMMENTS:** • Reconsider quality of Yi et al., and Roper et al., papers. ○ The Yi et al., paper is therefore of questionable quality and should be reconsidered in favor of Roper et al., (p. 118)	The Yi et al., paper has been removed from discussion and replaced with (Roper et al. 2007). EPA was unable to validate the data that was reported second-hand from Yi et al., which cited (Roper et al. 2007). The primary data from (Roper et al. 2007) was used instead.
SACC	**SACC COMMENTS:** • Evaluate assumptions related to reliance on OSHA PNOR standard for estimating dust exposure during building demolition versus monitoring data. • In addition, EPA's estimates of exposure to dust generated during building demolition do not rely on monitoring data but instead on the OSHA's Particulates Not Otherwise Regulated (PNOR) standard. While EPA's assessment may be conservative in assuming 100% of the dust up to OSHA's PNOR Permissible Exposure Limit (PEL) is HBCD, there is concern that demolition sites may routinely exceed nuisance dust standards and, therefore, EPA underestimates exposures to dust. (p. 118)	As discussed in Section 2.4.1.10 of the final Risk Evaluation, EPA is uncertain the OSHA PEL for PNOR represents actual dust inhalation exposure concentrations pertaining to workers during the demolition of buildings and other structures. Also, EPA evaluated information in specific references to information sources included in comments by the SACC or the general public on the draft HBCD Risk Evaluation. A reference by a public commenter to a specific information source is the reference to EPA's lead rule and the dust generation studies that EPA commissioned to measure total dust during various construction and demolition activities. EPA determined these studies are the following: (1) U.S. EPA. (2007). Revised Final Report on Characterization of Dust Lead Levels After Renovation, Repair, and Painting Activities. Prepared for EPA's Office of Pollution Prevention and Toxics (OPPT). Available online at: https://www.epa.gov/lead/revised-final-report-characterization-dust-lead-levels-after-renovation-repair-and-painting (2) U.S. EPA. (2014). Approach for Estimating Exposures and Incremental Health Effects from Lead due to Renovation, Repair, and Painting Activities in Public and Commercial Buildings.

		SAB Review Draft, July 25, 2014. Office of Pollution Prevention and Toxics. Available at: https://www.epa.gov/lead/approach-estimating-exposures-and-incremental-health-effects-lead-due-renovation-repair-and Some but not all the renovation and repair activities mentioned in the first study referenced above may be relevant to the assessment of worker exposure to dust resulting from demolition of structures containing XPS/EPS insulation. The activities that may be relevant include cut outs, kitchen gut, window replacement, trim/soffit replacement and door replacement; the activities that are irrelevant are door scraping, dry scraping, heat gun, power sanding, torch burning, and needle gun paint removal. However, the study includes lead air concentrations but does not include total particulate air concentrations. The second study referenced above also does not include total particulate air concentrations and therefore the data reported in the two studies are not useful for the evaluation of the validity of EPA's assumption. In conclusion, EPA's considerations did not result in a change of assessment method and EPA kept the estimation of HBCD inhalation exposure concentration based on the OSHA PEL for PNOR in the final Risk Evaluation.
SACC	**SACC COMMENTS:** • Contact NIOSH for information that may increase reliability of exposure estimates for construction sector. o The Committee recommended that EPA contact NIOSH's National Center for Construction Safety and Health Research and Translation as a potential source of information for work practices and exposures in the construction sector that may help increase the reliability of exposure estimates. (pp. 118-119)	EPA responded to the comment by searching the main webpage associated with NIOSH's construction and health resources and by reviewing the links and available documents on the webpage. EPA specifically searched for information related to dust emissions and worker inhalation exposure monitoring data during demolition activities. EPA did not find information related to dust emissions during demolition activities during these searches. EPA found worker inhalation exposure monitoring data

		during construction and demolition activities; however, these data were for specific compounds, such as crystalline silica and polychlorinated biphenyls, and specific activities, such as cutting cement, that were not applicable to HBCD and the conditions of use in the RE.
#	**Summary of Public Comments for Specific Issues Related to Charge Question 5**	**EPA/OPPT Response**
General		
59 62 55 58	**PUBLIC COMMENTS:** • EPA underestimates exposure to workers by: o Excluding known sources of exposure such as "reuse, disposal, and recycling of HBCD-containing products from legacy uses…" and "high impact polystyrene (HIPS) for electrical and electronic appliances, consumer and commercial textiles, adhesives, coatings, children's products including toys and car seats; furniture (such as bean bag chairs). o Not aggregating exposures. o Making assumptions and not providing justification or supporting data for those assumptions. o Neglecting to consider scientifically established factors that contribute to susceptibility. • EPA assumes that workers will be exposed up to but not in excess of OSHA's permissible exposure limit ("PEL") for nuisance dusts (15 mg/m3) and that the concentrations of HBCD within that dust will be proportionate to percentage of HBCD by weight in insulation (0.7-2.0%). o EPA should provide support for these assumptions. • EPA notes that environmental and occupational exposures to HBCD may occur during compounding of polystyrene resin to produce XPS Masterbatch (Sections 2.2.3 and 2.4.1.3) and subsequent manufacture of XPS Foam using XPS Masterbatch (Sections 2.2.4 and 2.4.1.4). EPA also notes that environmental and occupational exposures to HBCD may occurring during manufacture of XPS Foam using HBCD Powder (Sections 2.2.5 and 2.4.1.5). • EPA estimates releases and exposures based on a processing volume of 100,000 pounds HBCD per site per year for both XPS manufacturing processes. o These estimates are conservative as there may not be any North	Due to the court ruling in Safer Chemicals Healthy Families v. U.S. Envtl. Prot. Agency, EPA has added conditions of use for the activities it had excluded as "legacy uses" and "associated disposals" in the draft risk evaluation. Exposure to HBCD from use, reuse, recycling, or disposal of discontinued products and articles is not excluded from the final risk evaluation. The Agency added new conditions of use for the commercial/consumer use and disposal of products and articles that are no longer processed using HBCD (Section 1.2.8). EPA did not aggregate occupational exposures because a PBPK model for HBCD is lacking, and the results of aggregation would be uncertain without a PBPK model as discussed in Section 4.4.2. EPA's responses to specific comments pertaining to EPA's assumptions are given below. The OSHA PNOR PEL model was used in the absence of relevant data for the Demolition and Disposal of XPS/EPS Foam Insulation in Residential, Public, and Commercial Buildings, and Other Structures. In addition, EPA performed a limited supplemental data search for surrogate data on occupational exposures during demolition. EPA was not able to identify reasonably available data that was similar to the conditions expected during demolition of insulation materials.

	American manufacture or import of XPS masterbatch made with HBCD, any XPS foam insulation manufacturers in North America still using HBCD, or importers of XPS foam insulation products still containing HBCD.	EPA acknowledges that the 100,000 pounds assumption may be conservative given the current status of HBCD manufacture and import, as noted in the Risk Evaluation. The use in EPS and XPS foam had accounted for 95% of all HBCD applications in the past decade. Furthermore, the XPS Association (XPSA) stated that its members, who are the major producers of XPS resin, supply the resin for more than 95% of the XPS foam insulation products manufactured for the North American market and indicated that the remaining small percentage is probably made using imported resin (XPSA, 2017a). This imported resin may contain HBCD, however, the extent to which EPA does not know. EPA decided to include XPS in the Risk Evaluation given past HBCD use and the fact that small quantities of HBCD containing resin could still be used by non-member companies (Section 1.2). As stated in the final Risk Evaluation, 100,000 pounds per year is an upper bound for the import volume for the unknown site, otherwise, the site would be out of compliance with CDR reporting requirements. To accommodate lower levels of HBCD volume for XPS, however, EPA also estimated releases and exposures for lesser amounts: 25,000 and 50,000 pounds per site per year (Section 2.2.1 Release Assessment Approach and Methodology).
55	• The central tendency scenario is not protective of workers. ○ It assumes a 31-year career (nine fewer than the OSHA default level), and exposure durations and concentrations that are not supported by the record. ○ EPA measures acute occupational inhalation risks using eight-hour time weighted average values, which are not reflective of peak exposures and impacts. ○ There are frequently times during the workday where normal	The assumed working years of a career is only relevant for calculations of lifetime cancer risk, which is not assessed for HBCD (see equations in Appendix E.3). For non-cancer risk, the working years of a career cancel out (they are in both numerator and denominator). There are no short-term acute hazards for HBCD that would be relevant to less than a full day of exposure, so peak exposures less than 8h duration are irrelevant for risk estimates.

	work activities can result in exposures far greater than the eight-hour average, and even brief exposures to those peak levels can have acute adverse health effects. ○ EPA should follow American Conference of Governmental Industrial Hygienists (ACGIH) standard practice, which is to identify the activity that generates the greatest peak exposure and to collect a fifteen-minute sample to evaluate short-term impacts.	
31, 51, 58	• Several studies on HBCD migration from polystyrene have established mass transfer values that EPA can use to improve the confidence in the inhalation model estimates. In the draft risk evaluation, EPA indicates it has "low to medium confidence" in the HBCD air concentrations resulting from demolition and disposal of EPS/XPS foam insulation products. ○ The draft risk evaluation describes the method used to calculate this value, beginning with the particles not otherwise regulated (PNOR) for total dust and then multiplying by the HBCD weight fraction of 2 and 0.7%, resulting in expected exposure levels of 0.105 to 0.30 mg/m3. ○ The low confidence results from the inability to determine the amount of HBCD available for uptake due to entrainment within the polymer matrix. ▪ Several studies have examined HBCD migration rates from insulation materials, including polystyrene insulating boards, and have calculated mass transfer rates. ▪ For example, an emission modeling report (Executive Summary attached to XPSA October 10, 2018 Comments noted above) prepared by consultant PSI Cube in Germany (Dr. Rainer Brandsch) modeled air emission of HBCD from PS foam using generally recognized diffusion models (based on Fick's 2nd law of diffusion and following migration modeling specified in the EU Plastics Regulation 10/2011). Modeling predicted cumulated total emission of HBCD to air over the 100-year service life of PS foam to be 175 µg/m2 of foam surface. EPA should incorporate these values into their calculations to arrive at exposure levels supported by scientific evidence, thus increasing the confidence in these modeled levels.	The Extruded Polystyrene Foam Association (XPSA), in their comment on the Draft HBCD Risk Evaluation, referred to EPA's statements that HBCD is entrained in polystyrene (PS) foam. The XPSA concurred with this statement based on the estimate of maximal HBCD emission rate from PS to any environmental medium that the XPSA mentioned in their comment. This emission rate is equal to 881 ng/m^2/day and was derived by estimating the diffusion rate of HBCD within PS foam. EPA's statements that the XPSA referred to are statements associated with the estimation of releases to the environment and occupational exposure. In some instances, these statements pertain specifically to the uncertainty of estimates of worker inhalation exposure to HBCD contained in dust that is composed of airborne particles of XPS or EPS insulation or XPS masterbatch. The reason for this uncertainty is that the HBCD in such particles may not be fully absorbed in the human body if HBCD remains entrained within foam particles. Nonetheless, based on available toxicokinetic data, HBCD particulates are expected to be either absorbed in the lungs or swallowed and then absorbed in the gut (Section 4.2.1). The American Chemical Council (ACC), in their comments on the Draft HBCD Risk Evaluation, recommended the incorporation by EPA of values of HBCD migration from PS foam to reduce uncertainty and increase confidence in EPA's estimate of worker HBCD inhalation exposure pertaining to demolition

		and disposal and referred EPA to Rauert et al., (2014) towards this end. The maximum HBCD specific emission rate or flux from PS foam insulation as measured in an emission chamber is 696 ng/m^2/day (Rauert, 2014). The total HBCD air concentration that workers may potentially be exposed to during demolition results from HBCD mass transfer from the PS foam to air (HBCD migration) and the generation of PS foam particles. The later effect is the basis for EPA's estimate of the HBCD inhalation exposure and EPA did not account for HBCD migration because the rate of migration is much less than the HBCD emission rate resulting from the generation of PS foam particles. As stated in the HBCD Risk Evaluation, the emission rate due to the generation PS foam particles during demolition in the case of residential and commercial buildings is 7.57E-04 kg HBCD /day and 0.675 kg HBCD /day, respectively (EPA lacks information about the extent to which such emissions are in the form of inhalable PS foam particles which are relevant to worker inhalation exposure.) In contrast, EPA estimates the maximum migration rate in the case of residential and commercial buildings to be 7.2E-07 and 5.7E-05 kg HBCD/day, respectively. EPA estimated these values as the product of the measured migration rate mentioned above or 696 ng HBCD/m^2/day and the total surface area of PS foam insulation (the surface area of the two sides and the edges.) The following is a sample calculation that pertains to commercial buildings: As stated in Section 2.2.9 of the final Risk Evaluation, 2,440 m^3 of XPS and/or EPS insulation with a thickness of 0.06 meters and hence a total surface area of one side of 40,733 m^2 is used at a commercial site. The total surface area from which migration occurs

		= 2*40,733 m^2 + 0.06m*4*(40,733 m^2)$^{1/2}$ = 81,514 m^2 The migration rate in the case of the demolition of commercial buildings = 696 ng HBCD/m^2/day * 81,514 m^2 = 5.7E-05 kg/day.
29 55	**PUBLIC COMMENTS:** • EPA relies on a series of studies that do not mention PPE use to determine the occupational exposure levels workers face. o EPA then discounts the reported exposure levels on the assumption that all workers are provided with, and use, appropriate personal protective equipment (PPE). ▪ Standard industrial hygiene practice, incorporated into every OSHA health standard promulgated since 1970, requires that employee exposure be measured without regard to respirator use. ▪ EPA must articulate why it departed from the well-established practice that worker exposure is measured without regard to respirator use in its determination of exposure levels for workers under various conditions of use. • EPA should consider other existing available worker exposure data. If data are not available, EPA should use its authority under TSCA to order the production or generation of information that is needed.	EPA generally assumes compliance with OSHA requirements for protection of workers, including the implementation of the hierarchy of controls. In support of this assumption, EPA used reasonably available information, including public comments, indicating that some employers, particularly in the industrial setting, are providing appropriate engineering or administrative controls or PPE to their employees consistent with OSHA requirements. EPA does not have reasonably available information to support this assumption for each COU; however, EPA does not believe that the Agency must presume, in the absence of such information, a lack of compliance with existing regulatory programs and practices. Rather, EPA assumes there is compliance with worker protection standards unless case-specific facts indicate otherwise, and therefore existing OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE in a manner that achieves the stated APF or PF. EPA's decisions for unreasonable risk to workers are based on high-end exposure estimates, in order to account for the uncertainties related to whether or not workers are using PPE. EPA believes this is a reasonable and appropriate approach that accounts for reasonably available information and professional judgment related to worker protection practices, and addresses uncertainties regarding availability and use of PPE.

		EPA evaluated all reasonably available data on occupational exposures to HBCD gathered by reviewing peer-reviewed literature and information collected from governmental agencies. EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to complete the HBCD risk evaluation using a weight of the scientific evidence approach in light of the limited time available under the statute for completing the risk evaluation. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation.
Exposure to ONUs		

55	**PUBLIC COMMENTS:**
	• The range of workers EPA defines as occupational non-users (ONUs) is too large to support a single classification.
	  ○ Additionally, no exposure data are available for workers who do not regularly handle or work with the chemical but work in or near areas where the chemical is handled (ONUs).
	
	• EPA assumes ONUs will be exposed to lower contaminant concentrations than direct users of HBCD.
	  ○ EPA must provide justification for assumed ONU exposure levels and evaluate risk based on reasonably available data for each specific type of ONU worker.
		EPA does not have reasonably available information and data to consider different categories of ONUs or to develop additional scenarios for ONU exposures. Examples of workers EPA estimated as ONU are provided in Appendix E.5 Approaches for Estimating Number of Workers and include such workers as supervisors whose job duties do not include handling HBCD but may be exposed as part of their job.
		
		The worker monitoring data identified through EPA's systematic review process are presented in Appendix E.1, Inhalation Monitoring Data Summary, and include personal and area monitoring data. These data do not pertain to the relevant ONUs for the following reasons: (1) the worker activities associated with the personal monitoring data are not relevant to ONUs, and (2) the area monitoring data and the data for

		which the type of sampling is not reported are either not relevant to the exposure scenarios or are not relevant to ONUs. For example, in the case of the data pertaining to the Compounding of Polystyrene Resin to Produce XPS Masterbatch Containing HBCD, which is 8-hr TWA data, the sampling location is the feed deck near typical operator positions. This data likely does not represent ONU exposure because an ONU is unlikely to be present at the feed deck for an entire shift. EPA assumes HBCD air concentrations that ONUs are potentially exposed to are lower than HBCD air concentrations that workers are potentially exposed to because the dust is diluted as it is transported through workspaces by indoor or ambient air currents. EPA also assumes the duration and frequency of the ONUs' potential HBCD inhalation exposures to be lower than that of workers. The lower HBCD potential inhalation exposure levels of ONUs would result in lower risk for ONUs as compared to workers.
Lack of Occupational Exposure Data/Insufficient Data		
43 55	**<u>PUBLIC COMMENTS:</u>** • EPA reported that it could identify no reasonable surrogates for dust creation from foam insulation during demolition; instead the agency relied on a default assumption of OSHA's PEL for PNOR. o A search identified numerous studies identifying air dust concentrations that demolition workers are exposed to in a wide variety of scenarios. Many showed average dust levels well above the default PEL, with some measurements orders of magnitude higher. o These studies should be reviewed to determine if there are reasonable surrogates for demolition of foam board. • The EPA cannot meaningfully evaluate risks to workers and occupational non-users (ONUs) because it lacks reliable occupational exposure data. o There is a lack of inhalation exposure air concentrations	EPA reviewed specific references to data presented by the public or peer review panel. The specific references to data were to EPA studies that are related to EPA's lead rule. EPA reviewed these studies and discussed the outcome of this review in the response to the comment above under Other Panel Recommendations. In addition, EPA performed a limited supplemental search for data pertaining to dust emissions and occupational exposure at demolition sites but did not find any reasonably available data. EPA conducted a Systematic Review of published literature and identified occupational exposure data

55	pertaining to workers in the U.S. o EPA does not have inhalation monitoring data for construction workers exposed to HBCD. o There are no discrete data points measuring worker exposures to HBCD. o ONU exposures were not quantitatively assessed in the risk evaluation due to "lack of data." • EPA relies on modeling exposure values, studies of foreign workplaces, and other data sources that are not considered to be representative of the broad range of U.S. work exposures including: o "Workplace exposure to HBCD in the European Union" that did not contain the underlying monitoring data or describe how the average values that EPA relied upon were calculated. ▪ Information on the conditions under which European HBCD monitoring was conducted must be obtained. ▪ The countries the HBCD inhalation data were taken from must be reported in the risk evaluation. Several European nations have lower occupational exposure limits than the U.S. and may understate U.S. worker exposure. ▪ Use of exposure data from Europe is likely to understate worker exposures in the U.S. due to different working conditions; these data do not provide substantial evidence for the determination of no reasonable risk. o Exposure estimates from a European Union risk assessment that "did not provide details about how these values were calculated" and did not contain the underlying data were used. ▪ How the average values cited in these sources were calculated needs to be verified. o This reliance on inappropriate surrogates in lieu of reasonably available and more reliable domestic monitoring data violates TSCA.	via this Systematic Review. EPA then evaluated the HBCD occupational exposure data identified using the data quality evaluation metrics developed for TSCA risk evaluations, as published in the Application of Systematic Review in TSCA risk evaluations. The HBCD occupational exposure data that EPA obtained does not include data pertaining to workers in the U.S. or for construction workers. The monitoring data used for occupational exposure estimates were all rated as high quality, and the uncertainty with use of international exposure information (including differences in occupational exposure regulatory limits) and lack of discrete data points is discussed and considered in the confidence of exposure estimates.
Exposures Not Addressed		
54, 62	**PUBLIC COMMENTS:** • EPA did not evaluate exposure of workers at transfer stations, landfills, and incinerators where HBCD wastes are received, or to firefighters who are the first responders when insulation and other products containing HBCD are burning.	The Risk Evaluation has been revised to discuss exposures to workers at waste management sites in Section 2.4.1.10. Demolition and Disposal of EPS/XPS Foam Insulation Products in Residential, Public and Commercial Buildings, and Other

62 62 31, 51	• EPA evaluated inhalation of dust for demolition workers, but it did not evaluate exposure of workers at transfer stations, landfills, and incinerators where HBCD wastes are received, or to firefighters who are the first responders when insulation and other products containing HBCD are burning. • Exposure to fugitive dust at landfills and transfer stations should be evaluated. • The draft risk evaluation acknowledges that workers face "greater exposure" than the general public.	Structures. EPA evaluated exposures to workers and ONUs for conditions of use within the scope as outlined in the HBCD Problem Formulation. The potential exposures for firefighters are discussed in Section 2.4.1.1.15 Assumptions and Key Sources of Uncertainty for Occupational Exposures. EPA did not identify data specific to HBCD through the initial systematic review. EPA performed a limited supplemental data search to find information on firefighter exposure to HBCD. EPA only found one source that sample for HBCD for settled dust on PPE, but the study did not detect HBCD. EPA provides a discussion of other identified literature in Section 2.4.1.1.15.5 Firefighter Potential Occupational Exposures found for other flame retardants and combustion by-products. EPA acknowledges that firefighter exposure to HBCD is an uncertainty in the risk evaluation. EPA did not do a bystander evaluation for consumers as the consumer's estimated exposure is the most conservative one. The bystander approach therefore is not relevant for the purpose of making a conservative estimate of exposure due to a consumer use.
29	**PUBLIC COMMENTS:** • EPA did not consider exposure from renovation and demolition of buildings with HBCD-containing insulation. • EPA must provide the rationale for exposure sources which are included and excluded in the risk evaluation.	EPA does consider exposures to workers from renovation and demolition of buildings in Section 2.4.1.10 Demolition of XPS/EPS Foam Insulation Products in Residential, Public and Commercial Buildings. The rationale for the sources of exposure for occupational workers were provided in the Scope of the Risk Evaluation for Cyclic Aliphatic Bromides Cluster and the Problem Formulation of the Risk Evaluation for Cyclic Aliphatic Bromides Cluster.
Oral Exposure		

55	**PUBLIC COMMENTS:** • EPA does not consider oral exposure for workers. ○ Studies have shown that nearly one in six workers inadvertently ingest hazardous substances through activities like biting their nails, touching their faces, or eating in an area where chemicals dusts can contaminate their food.	EPA generally does not evaluate occupational exposures through the oral route. Workers may transfer chemicals from their hands to their mouths. The frequency and significance of this exposure route are dependent on several factors including the physical and chemical properties of the substance during worker activities, the visibility of the chemicals on the hands while working, workplace training and practices, and personal hygiene that is difficult to predict (Cherrie et al., 2006).
Aggregate Exposures		
59	**PUBLIC COMMENTS:** • EPA does not aggregate inhalation and dermal exposures for workers, instead calculating the risks separately. ○ EPA states that "Combining exposure routes would entail too much uncertainty given the lack of a usable physiologically based pharmacokinetic (PBPK) model"; however, these exposure routes are combined in the calculation of risk for the general population, so it is unclear why this cannot be done for workers.	EPA thanks the commenter for this insight. While there is significant uncertainty and potential for overestimation of dermal exposure based on use of an upper-end absorption estimate, this is a very minor contribution to the overall general population exposure and the additional dermal contribution is unlikely to overload toxicokinetic processes. For workers however, dermal exposure estimates are significantly higher than inhalation exposure and it would therefore be inappropriate to add a likely highly overestimated value to the inhalation exposure estimates without the use of a PBPK model available for determining the effect on internal dose estimates. Therefore, EPA chose not to employ simply additivity of exposure pathways for workers because of the uncertainties present in the current exposure estimation procedures.
59	• Background exposures, which EPA acknowledges are experienced by everyone, should be integrated for workers; some workers may also be consumer product users or be exposed to HBCD in drinking water and so there should be an additional calculation for this population.	For HBCD risk evaluation, EPA does not believe exposures need to be integrated for workers with the estimated background and consumer exposures, as the exposures estimated to be experienced by workers are significantly higher than background and consumer exposures. Therefore, risk calculated for workers that accounted for background or consumer exposure would have minimal to no effect on risk estimates.

Environmental, General Population, and Consumer Exposure – Public and Peer Review Comments		
Charge Question 6.1: Exposure modeling tools may have different levels of screening capacity such that one might be more conservative than another given the scenario and inputs. Please comment on EPA's approach to use a tiered method for identifying and prioritizing exposure scenarios to be subjected to higher screening level modeling tools, based on their potential for risk by first using a lower screening level tool. **Charge Question 6.2:** Please comment on EPA's approach to use receptor-specific exposure factors and activity patterns to estimate doses. **Charge Question 6.3:** Surveys have identified fish consumption rates far above those used in this draft risk evaluation to estimate dietary exposure for subsistence fishing populations. Please comment on the use of such information in estimating the contribution of fish and other aquatic life to dietary exposure to HBCD. **Charge Question 6.4:** Exposure modeling results may rely on various estimated inputs and ranges (*e.g.*, physical-chemical properties) given the available data, which results in variability and uncertainty in the results. Please comment on EPA's approach to qualitatively characterize variability and uncertainty for exposure estimates in Tables 2-111 and 2-112.		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 6**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 6.1		
Panel Recommendations (statements identified by committee that require clarification and/or further justification; contractor's paraphrased recommendation in bold)		
SACC	**SACC COMMENTS:** • The Committee concluded that further justification is needed to support the assumption of 75% removal in onsite wastewater treatment. (Section 2.3.7 Sensitivity Analysis – Environmental Exposure) • On Page 171: "Reported mean (67%), median (81%), minimum (-29%) and maximum (99%) values for total suspended solids (TSS) removal were reported for 39 observations. EPA considered these reported values and uncertainty in extrapolating from performance of the treatment systems surveyed in the Effluent Guidelines document to those facilities using HBCD. • EPA also considered uncertainty associated with the use of TSS removal as a surrogate for HBCD removal. EPA selected 75% removal of HBCD in onsite wastewater treatment for direct dischargers. EPA is confident that some removal of HBCD will occur in onsite wastewater treatment. Higher or lower removal of HBC could occur based on the type of treatment employed and its	EPA has provided an alternative percentage removal (90%) and the justification for the use of 90% removal efficiency for HBCD in POTWs in Section 2.3.6.4.

	performance optimization." (p. 121)	
SACC	**SACC COMMENTS:** • Provide rationale for not including persistence and longer-term sinks in the modeling of HBCD concentrations in water and sediment OR Reconsider applicability of accumulation and long-term release of HBCD (Section 2.3.8 Assumptions and key sources of uncertainty in environmental exposure assessment) • Page 173: "When modeling the HBCD concentrations in water and sediment, EPA did not consider the potential impact of persistence and longer-term sinks in lake and estuary environments." The Committee found this statement in direct contradiction to the understanding that HBCD is persistent and bioaccumulative. A rationale for not including persistence and longer-term sinks in the modeling of HBCD concentrations in water and sediment should be provided in the Evaluation. The Committee considered accumulation and long-term release of HBCD would clearly be the most directly applicable to obtaining good estimates of exposure. (pp. 121-122)	EPA modeled HBCD surface water and sediment concentrations using half-lives. A half-life is a parameter that informs how long a chemical will persist in the environment before degrading. EPA acknowledges this statement and the sentence was deleted. Various bodies of water were represented in the monitoring data including lakes for example, that represent long-term sources. The statement was made in reference to the PSC model and its ability to consider long term sink effects.
SACC	**SACC COMMENTS:** • . . . this Evaluation is likely to underestimate exposure to both the general population and consumers. It is critically important that this risk evaluation incorporate extensive and reliable monitoring data and that the assumptions underpinning exposure modeling are carefully considered and reviewed. (p. 99)	EPA incorporated aggregate exposures covering all potential exposure routes for the general population and consumers. EPA also estimated risk for additional PESS groups including infants (including above the 99.9%tile of modeled exposure) and subsistence fishers. It is therefore unlikely that EPA underestimated total exposures to these groups.
SACC	**SACC COMMENTS:** • Each of the models used in this Evaluation are complex in construction and incorporate multiple assumptions. Only modeling experts can truly assess the impact on model outputs when reality deviates from modeled assumptions. The Committee expressed additional experts were needed to assess the adequacy and appropriateness of use for each model. The Committee recommended that once EPA has utilized these models for the evaluation of several chemicals under TSCA, that a panel of modeling experts be convened	EPA acknowledges this comment.

	to assess the conservativeness of model estimates. (p. 121)	
SACC	**SACC COMMENTS:** (Section 2.4.2.1 Approach and methodology) • On Page 221: "In this evaluation, general population is considered to be individuals who are not expected to live close to point sources (far-field) and are not expected to have HBCD-containing articles in their home, although data on the prevalence of articles containing HBCD in homes throughout the United States is not well characterized." Given the absence of data from the U.S., and the long-term wide-spread use of HBCD in household use materials, the Committee recommended EPA provide a rationale for this assumption. (p. 122)	EPA has revised the paragraph to read: "Risks were estimated for the general population, representing steady-state chronic risks from sustained background exposure in the environment due to HBCD persistence. In this assessment, general population is considered to be individuals who are not living close to point sources (*i.e.*, industrial facilities that release HBCD) and do not have a specific source within a living environment that has been assessed by EPA in the consumer exposure assessment (*i.e.*, home, auto-components, mouthing of recycled products). HBCD exposures to the general population may be variable as they are influenced by both sources into the environment, degradation and removal from the environment. Estimates of general population exposures based on environmental monitoring and biomonitoring data represent the conditions present at the time the data was collected. It is unknown which combination of potential sources associated with conditions of use as described in this risk assessment contribute to the monitoring data presented here. However, given the wide range of exposures shown within and across the monitoring data, there is a plausible contribution from some of the sources/conditions of use described within this document. These exposure estimates serve as a baseline onto which any exposure scenario-specific modeled releases will be added."
SACC	**SACC COMMENTS:** (Section 2.4.2.1 Approach and methodology) • On page 221: EPA describes exposure to the general population as "more homogenous as this group is exposed primarily to background levels of HBCD" yet page 226 states "HBCD exposures to the general population are highly variable and are influenced by both sources into the environment and degradation and removal from the environment."	EPA will revise the statements so that they are consistent. The wording changed to this: "Although general population estimates may be variable, they are expected to be more homogenous than the highly-exposed group(s), which have a wider range of exposure estimates due to the various scenario-specific water, air, and/or consumer article

	The Committee recommended EPA consider re-wording one or the other to be consistent. (p. 122)	releases assessed.
SACC	**SACC COMMENTS:** (Section 2.4.2.2 General population exposures from environmental monitoring and exposure factors and from human biomonitoring and reverse dosimetry) • On Page 226: The 64-day half-life attributed to Aylward and Hays (2011) is a secondary citation to Geyer et al., (2004). Geyer et al., estimated a range of 23-219 days. The Committee recommended incorporating the uncertainty of the primary reference into the risk evaluation. (p. 122)	EPA attempted to attribute the 64-day half-life to Geyer et al., (2004) and described the uncertainty in the value. Upon review of Geyer et al., (2004), it appears that the range of 23-219 days is based on concentrations from an article which is a conference abstract. The conference abstracts were excluded in Systematic Review.
SACC	**SACC COMMENTS:** • **Provide labeling on X-axes of figures** (Section 2.4.2.2 General population exposures from environmental monitoring and exposure factors and from human biomonitoring and reverse dosimetry) • On pages 229, 237, 238, the X-axes in figures 2-2 through 2-5 require labels. (p. 122)	These figures have been removed from the risk evaluation and therefore no further edits are required.
SACC	**SACC COMMENTS:** (Section 2.4.2.3 Dietary exposure) • Page 231: "The levels of HBCD present in these food groups are typically lower than levels detected in wild animals and in plants." How does this finding impact the dietary exposure analyses performed? (p. 122)	EPA acknowledges that these subsistence dietary scenarios could add an additional layer of uncertainty to the general population dietary analysis. This was added to the uncertainty section: Also, the subsistence fisher subpopulation's dietary exposures to HBCD were estimated with the assumption that fish ingestion was the main driver of HBCD exposure. This does not account for other wild animals or wild edible vegetation that may be additional sources of dietary HBCD.
SACC	**SACC COMMENTS:** Include dietary consumption of bottom feeding fish (Section 2.4.2.3 Dietary exposure) • Page 233: The dietary exposure analysis should include consideration of dietary consumption of bottom feeding fish (*e.g.*, catfish) which are	EPA used the highest fish tissue concentration from the Chen (2011) paper and the highest fish concentration was from common carp and this was used for the subsistence fishing population. Catfish, crabs, crustaceans, and shellfish including oysters, clams, and mussels, typically bottom-feeding or filter feeding fish, were included in the reported market

	likely to accumulate higher levels of HBCD from sifting through sediment and therefore present higher exposure risk to humans who consume them. (p. 122)	basket studies.
SACC	**SACC COMMENTS:** (Section 2.4.2.3 Dietary exposure) • Page 233: EPA chose a BAF value at the lower end of the reported range. The rationale given was that the model-based dissolved surface water estimates were "generally larger" than reported values, so choosing a higher BAF with a higher water estimate would give "unreasonably high estimated fish-tissue concentrations. Is there any data to support this assumption? (p. 122)	Section 2.4.3.2 and Table 2-95: The modeled concentrations that use the lower-end BAF values are below the monitored values, thus the lower BAF value is more appropriate. The high-end of the range for fish tissue concentrations is an order of magnitude lower than the modeled concentrations.
SACC	**SACC COMMENTS:** (Section 2.4.2.3 Dietary exposure) • Page 234: "EPA compared the range of reported fish-tissue concentrations from monitoring data and found the modeled fish tissue concentrations (range of modeled dissolved surface water and low-end lipid normalized upper trophic level fish BAF) to be of a similar order of magnitude." Provide actual ranges of orders of magnitude rather than use the subjective modifier "similar." (p. 122-123)	EPA has provided ranges of estimates for the various methods in Table 2-95 to allow for comparison.
SACC	**SACC COMMENTS:** (Section 2.4.2.3 Dietary exposure) • Page 234: "Across all samples, mean HBCD concentrations ranged from ND to 22 g/kg lw in 1999-2002 samples and increased to 13 to 4,640 g/kg lw. Assuming 10% lipid, this converts to $1.3e^{-6}$ µg/mg ww to $4.64e^{-4}$ µg/mg ww." This suggests that ww concentrations may not be declining as use is declining. How is this justified with the assumption that environmental concentrations are decreasing? This should also be factored into the discussion on uncertainties. (p. 123)	This study is a more local study and the author believes that a new point source might have been added. However, the author does not demonstrate that this data is representative of a nationwide assessment.
SACC	**SACC COMMENTS:** (Section 2.4.2.3 Dietary exposure) • Page 235, Table 2-78 and Table 2-93 on page 259: Estimated concentrations in water appear to be an order of magnitude lower than	EPA checked and the values are correct. Table 2-61 has surface water concentrations for the 7Q10 50th flow. 7Q10 flows are lower than the mean flows and therefore should be lower than those used human fish

	reported in Table 2-54 on page 160. This should be checked, and differences justified if found to be correct. (p. 123)	ingestion estimates summarized in Table 2-95.
SACC	**SACC COMMENTS:** (Section 2.4.2.3 Dietary exposure) • Page 242: In Table 2-80 it appears that the concentration in fish captured near the point source are lower than the high range concentration values in fish captured far from the point sources. On page 234 EPA cites Chen et al., (2011) as finding concentrations in fish captured near point sources were generally 1 to 2 orders of magnitude higher than fish captured further away from sources. These two pieces of information need to be rectified and discussed. Further explanation of Table 2-80 needs to be added to the text. (p. 123)	Table 2-80 (now Table 2-95) was modified to show the range of all studies combined, and the text was modified to provide a paragraph that was described the data, including representative near and far studies. In Table 2-80 some of the studies of fish captured further away from sources included samples collected in industrial areas.
SACC	**SACC COMMENTS:** (Section 2.4.2.4 Dust and soil ingestion) • Page 246: The summary of soil concentration ranges provided in Table 2-84 appear to be different from the environmental assessment summary ranges provided in Table 2-56 on page 167. These differences need to be explained. The references in the two sections are the same, that is Tang 2014a and Tang 2014b refer to the same paper. (p. 123)	In the final risk evaluation, the summary of monitoring data values match between tables. Data for individual studies have been removed in the summary tables.
SACC	**SACC COMMENTS:** (Section 2.4.2.4 Dust and soil ingestion) • Table 2-83 on page 245: As with most exposure evaluations carried out for regulatory purposes, this Evaluation excludes soil ingestion rates by children exhibiting soil pica – a relevant susceptibility. The Evaluation should make this explicit in the text. (p. 124)	EPA only assessed incidental ingestion of soil, not pica. Soil ingestion even in the case of pica is expected to be a very minor contributor to the aggregate general population exposure relative to indoor dust and diet.
SACC	**SACC COMMENTS:** (Section 2.4.2.7 qualitative exposure scenarios) • Page 257: In the section labeled HBCD sent to Landfill Across the Lifecycle, the Evaluation implies that total releases are expected to be large for years to come. Spreading the total tonnage out over the total number of landfills likely to accept these materials brings the concentration down to the central tendency estimates derived for	EPA has updated landfill leachate discussion, now section 2.4.5.2, to address comments, considering literature references for assumptions.

	extracted soil monitoring data. Also assumed is that landfill releases are mitigated by coverings, liners and treatment. As mentioned in public comments,[11] this may be an overconfident assumption. For this reason, additional uncertainty factors should be considered. (p. 123)	
Summary of Peer Review Comments for Specific Issues Related to Charge Question 6.2		
SACC	**SACC COMMENTS:** • Obtain monitoring data to ground-truth those E-FAST predicted exposure values that exceeded an acute or chronic hazard value. • EPA applied the more complete partitioning Variable Volume Water Model-Point Source Calculator (VVWM-PSC) only for scenarios where the Exposure Fate Assessment and Screening Tool (E-FAST) predicted exposure value that exceeded an acute or chronic hazard value. Interestingly in this case, most of them did exceed the hazard value. It is important to ground-truth these predictions with monitoring data. (p. 124)	In the revised assessment EPA provides a table (2-63) that compiles the modeled and measured concentration.
SACC	**SACC COMMENTS:** • Evaluate peer review recommendations for Charge Question #4 for relevance to Charge Question 6.1. • The comments and suggestions to Charge Question 4 are also relevant to this question (p. 124) with respect to half-lives and production volume selection and uncertainty analysis.	For the HBCD final risk evaluation, EPA performed two sensitivity analyses, varying HBCD half-lives and production volume for select exposure scenarios. The rationale for the sensitivity analysis for production volume is provided in Section 2.2.15. EPA selected two lower production volumes as a possibility existed that an unidentified site could manufacture or import at any volume below 100,000 lbs/yr. These were carried forward to environmental exposure estimates. For this assessment E-FAST is considered to be a screening level tool that provides surface water concentrations regardless of fate properties *e.g.*, half-life, whereas the VVWM-PSC model does take these properties into account. The former model is a higher throughput, more conservative model than the latter model, which is

		why EPA prioritized only those scenarios that underwent E-FAST and exceeded the COC for lower throughput more conservative modeling.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 6.3		
SACC	**SACC COMMENTS:** • The Committee was unable to determine if the sensitivity analysis for infant exposures by consideration of varying percentiles is valid (Figure 2-6 p. 273). The Committee recommended that this analysis be reviewed by a statistician familiar with population exposure modeling. (p. 124).	This sensitivity analysis was intended to confirm that EPA's risk evaluation was protective of even the most highly exposed infants. With risk estimates for infants several orders of magnitude above benchmark and the risk estimates based on the maximum modeled dose above the 99.5 percentile of potential exposure still above benchmark, these results confirm that HBCD is not a risk to infants in the general population and any small adjustments would not be expected to affect the risk conclusions. EPA will look to incorporate advice and recommendations for improving statistical models into future risk evaluation analyses.
SACC	**SACC COMMENTS:** • Apply recommendations from Charge Question #5 for modeling dermal absorption for occupational exposures to general population exposures. • The discussion and associated recommendations related to modeling of dermal absorption for estimating Occupational Exposures also apply to General Population exposures. (p. 124)	Both occupational, general population, and consumer exposure assessments used a fractional absorption method, albeit with different assumptions for quantity deposited on the hand and other parameters. 6.5% absorption was applied for each, based on data from Abdallah et al., (2015). A comparison of estimated absorption via both fractional absorbed and permeability methods has been added to Appendix L. As for overall exposure modeling, the occupational assessment considers only dermal exposure via the hands, while exposure to the general population either outside or within the home can occur across the entire body. The general population exposure assessment assumed "that exposed body parts are hands, lower legs (45% of total leg), and lower arms (50% of lower arms). Workers are likely to be covered by clothing on arms and legs. Therefore, the two assessments are not equivalent and cannot be applied to each other.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 6.4		

SACC	**SACC COMMENTS:** • The Committee concluded that to be protective and account for susceptible population, the Evaluation should consider the use of consumption rates on the high end when estimating exposures. One Committee member recommended the EPA look at three papers by Lee et al., (2019), Cao et al., (2018), and Fromme et al. (2016) that address dietary exposure and risk management. (p. 125) ○ Lee CC, Chang WH, Chen HL. 2019. Environmental Pollution 249. pp 728-734. doi: 10.1016/j.envpol.2019.03.040. Epub 2019 Mar 14. - Dietary exposure and risk assessment of exposure to hexabromocyclododecanes in a Taiwan population ○ Cao X, Lu Y, Zhang Y, Khan K, Wang C, Baninla Y. 2018. Environmental Pollution. 236. pp:283-295. doi: 10.1016/j.envpol.2018.01.040. A review of hexabromocyclododecanes (HBCDs) in environmental media with focus on their potential risk and management in China. (p. 142) • Fromme H, Hilger B, Albrecht M, Gries W, Leng G, Völkel W. 2016. Int J Hyg Environ Health. 219(4-5). pp 380-8. doi: 10.1016/j.ijheh.2016.03.003. Occurrence of chlorinated and brominated dioxins/furans, PCBs, and brominated flame retardants in blood of German adults	EPA used central and high-end concentrations and ingestion rates from grey literature sources such as the Exposure Factors Handbook and guides from EPA's Office of Water. Lee et al., 2019 was not part of EPA's initial data extraction effort because it was published after the literature search cutoff date (Feb 2017) established by the systematic review process. However, EPA has reviewed the paper and provided a comparison of the dietary exposure estimate calculated by Lee et al, 2019 with those calculated by EPA on page 308 of the EPA Risk Evaluation. Lee et al., 2019 calculated exposure estimates using concentration and consumption rates specific to the Taiwanese population, resulting in mean estimated daily intakes (EDI) ranging from 3.8E-7 to 1.58E-6 mg/kg/day, which are similar or lower than the EPA central and high-end estimates ranging from 2.3E-6 to 8.1 E-5 mg/kg/day. Cao et al., 2018 was not initially included in EPA's data extraction effort because it was published after the literature search cutoff date (Feb 2017) established by the systematic review process. However, EPA has reviewed the paper and provided a comparison of the dietary exposure estimate calculated by Cao et al., 2018 with those calculated by EPA on page 308 of the EPA Risk Evaluation. Cao et al., 2018 calculated exposure estimates using concentration and consumption rates specific to the South China population, resulting in an mean EDI of approximately 5E-7 mg/kg/day (rough interpretation from graph), which is lower than the EPA central and high-end estimates ranging

		from 2.3E-6 to 8.1 E-5 mg/kg/day. Fromme et al., 2016 does not have consumption rates or dietary exposure estimates. Another related study, "Brominated flame retardants – Exposure and risk assessment for the general population" (Fromme 2015), is a secondary source of dietary exposure estimates and reports estimates ranging from 1.2E-7 to 5.9E-6 mg/kg/day, which are similar or lower than the EPA central and high-end estimates ranging from 2.3E-6 to 8.1 E-5 mg/kg/day.
SACC	**SACC COMMENTS:** • Based on the physical-chemical properties of HBCD, exposure to fish by HBCD in suspended particles could represent a substantial source of exposure, particularly for bottom-feeding fish. This exposure pathway should be acknowledged and discussed in the Evaluation. (p. 125)	EPA used the highest fish tissue concentration from the Chen (2011) paper and the highest fish concentration was from common carp. Channel catfish, typically a bottom-feeding fish had lower values.
SACC	**SACC COMMENTS:** • The Committee discussed two susceptible populations that are not adequately considered in the Evaluation, namely, high fish consumers and infants consuming breast milk. Because HBCD is a PBT, the fish consumption rates used in the scenarios are too low to protect high fish-consuming populations (Native Americans, Asian/Pacific Islanders, etc.). The breast milk pathway is identified in the Evaluation, but not emphasized and not discussed for high fish-consuming and lactating women. For example, Table 2-79, page 239 states that acute dose rates and average daily doses for fish ingestion excludes infants. Exposure pathways for both high fish consumers and infants consuming breast milk should be discussed. (p. 125)	Both infants and subsistence fishers are PESS and are captured in the risk evaluation. EPA acknowledges that breastmilk concentrations may be higher in women who consume more fish. EPA did an infant sensitivity analysis to capture high-end exposure up to and exceeding the 99th percentile, which would account for very high-end breast milk exposure. EPA excluded the direct consumption of fish for infants, with the assumption that breast milk is the main dietary source of HBCD for infants. Based on public and SACC comments, EPA has added risk estimates for subsistence fishers based on monitored fish concentrations and estimated increased fish ingestion rates (see Section 2.4.2.5 and 4.2.3.2).

Summary of Peer Review Comments for Specific Issues Related to Charge Question 6.5		
SACC	**SACC COMMENTS:** • In the Evaluation, the quantitative assessment of uncertainty and variability was presented in Tables 2-109 and 2-110. The Committee found these tables quite helpful in capturing and communicating EPA's thinking regarding contributions to uncertainty. As has been previously mentioned, the Committee recommended that definitions or descriptions of the "High," "Moderate" and "Low" modifiers of uncertainty and variability must be provided for these tables to be truly useful. (p. 125)	Table 2-114 now contains a qualitative assessment of uncertainty and variability based on the uncertainty and variability of environmental release, fate, and exposure estimation parameters.
SACC	**SACC COMMENTS:** • The Committee responses to other charge questions also addressed issues of uncertainty and variability and answers to these questions may require modifications to Table 2-109 and 2-110. (p. 126)	See response above.
#	**Summary of Public Comments for Specific Issues Related to Charge Question 6**	**EPA/OPPT Response**
Exposure Aggregation		
24, 57 53	**PUBLIC COMMENTS:** • EPA should combine general population exposure resulting from HBCD's releases into the environment with consumer exposure from HBCD-containing products as these two pathways of exposure affect the same people and thus should be aggregated to assess overall risk. • Potential cumulative and synergistic effects caused by HBCD and other persistent organic pollutants, particularly in traditional foods of Alaska Native peoples, should be considered. • People of the north may be at higher risk to exposures through indoor air and dust because of greater periods of time spent indoors because of the long winters, low ventilation, and greater insulation of homes against the cold.	For each consumer exposure scenario, EPA aggregated the affected pathway from the consumer scenario (*i.e.*, indoor air, dust, and/or mouthing) with the remaining pathways from the general population scenario. See Scenarios C1, C2, and C3 in Section 2.4.4. EPA acknowledges this statement; a tribal assessment was not conducted. However, EPA did perform risk estimation for subsistence fishers, a subpopulation that is similarly highly exposed due to increased fish consumption relative to the general population. While fish consumption for certain tribal communities may exceed even that of subsistence fishers, EPA assumes that these risk estimates are applicable to most communities. For insulation in house scenario (now C1), both

		central and high-end estimates of time spent indoors was used, as estimated through analysis of the EPA CHAD database. For the high-end scenario this amounted to 20 hours inside the home, 1 hour in the car, 1 hour in a commercial establishment, and 2 hours outside. For the house scenario, EPA modeled a generic house with insulation installed in a vented attic and crawl space. The HBCD source was 10 cm thick unfaced polystyrene insulation boards containing 0.5% HBCD. See Appendix G5 for details on IECCU modeling.
62 59 59 30, 54, 56	**PUBLIC COMMENTS:** • Drinking water was not evaluated as an exposure pathway in the risk evaluation. EPA states that "[f]urther analysis was not conducted for the drinking water pathway based on a qualitative assessment of the physical chemical properties and fate of HBCD in the environment." o EPA must specify what these properties are. o EPA states that "monitored levels of HBCD in drinking water are unavailable." o The absence of data does not excuse EPA from considering the risks posed to the general population by HBCD in drinking water. ▪ EPA chose not to collect such data under TSCA or the Safe Drinking Water Act. • The draft risk evaluation does not accurately identify or ensure the protection of populations with greater exposures because numerous known exposure sources were not evaluated. • EPA's risk determinations are not protective of potentially exposed or susceptible subpopulations. o EPA does not account for biological factors that can increase susceptibility to chemical toxicity. o EPA should identify people living in proximity to sources of HBCD contamination as potentially highly exposed or susceptible subpopulations. • EPA should evaluate exposure to HBCD through disposal pathways.	HBCD is not expected to partition and remain in surface water based on physical/chemical and fate properties and therefore this pathway did not undergo any additional analysis in the final Risk Evaluation. In the draft risk evaluation EPA evaluated various potential exposure routes, including inhalation of outdoor and indoor air, dust, dermal, fish ingestion, and other dietary sources. As stated above, HBCD does not partition to water for drinking water exposure. EPA identified subpopulations that are of higher exposure as well as subpopulations that have greater susceptibility and the factors affecting that susceptibility (Section 4.4.1). For the final risk evaluation, these sections have been split to the exposure and human health hazard sections, respectively. Section 4.4.1 details how these PESS were accounted for in the risk evaluation, including: providing risk estimates for both adult workers and women of childbearing age, risk estimates for all lifestages, risk estimates for highly exposed general population, and modeling the 99.9%tile of aggregate infant exposure. Additionally, for the final risk evaluation EPA added risk estimates for subsistence fishers. EPA created a separate "highly exposed general population" section with estimates specifically for

	The lack of evaluation of water release from leachate and surface water dust deposition from demolition and disposal sites underestimates the potential ingestion exposures that tribal people may have in depending on local fish for their nutritional sustenance.	PESS groups living close to facilities or exposed as consumers. Dust emissions from landfills and its impact on general population would be driven by many unknown factors: including, but not limited to the amount of HBCD-containing materials at the landfill, availability of HBCD containing materials at the surface, and size of landfills. The largest source of HBCD waste to landfills is expected from the demolition of buildings, EPA estimated this amount per year in Section 2.2.10. EPA did not calculate an average amount of HBCD waste per landfill as EPA expects the rates of demolition will vary between regions with certain areas having high rates of buildings renovation/demolition and the distribution of HBCD waste disposed between landfills would therefore be expected to vary. EPA provides a qualitative discussion of HBCD in landfill leachate and potential for exposure in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle. EPA did not address landfill debris in the final risk evaluation. EPA also did not evaluate HBCD releases from landfills that are covered by RCRA regulations because potential releases are expected to be mitigated by these regulations (Section 1.4.2.2) As explained in more detail in section 1.4.2 of the risk evaluation, EPA believes it is both reasonable and prudent to tailor TSCA risk evaluations when other EPA offices have expertise and experience to address specific environmental media, rather than attempt to evaluate and regulate potential exposures and risks from those media under TSCA. EPA believes that coordinated action on exposure pathways and risks addressed by other EPA-administered statutes and regulatory programs is consistent with statutory text and legislative history, particularly as they pertain to TSCA's function as a

		“gap-filling” statute, and also furthers EPA aims to efficiently use Agency resources, avoid duplicating efforts taken pursuant to other Agency programs, and meet the statutory deadline for completing risk evaluations. EPA has therefore tailored the scope of the risk evaluation for HCBD using authorities in TSCA Sections 6(b) and 9(b)(1).
Exposure to Children		
62 59 62	**PUBLIC COMMENTS:** • In estimating children’s exposures to HBCD from the mouthing of toys and other articles, EPA assumes only 8–15 minutes of mouthing exposures per day, for no more than 250 days over a single year of the children’s life. ○ EPA did not state how it derived those figures, which are significantly lower than the research-based mouthing values recommended in EPA’s Exposure Factors Handbook. ○ For high-end (95th percentile) exposure scenarios, the Handbook recommends the use of 26 minutes of object-to-mouth mouthing per hour for children 3–6 months of age, 19 minutes of object-to-mouth mouthing per hour for children 6–12 months of age, and 22 minutes of object-to-mouth mouthing per hour for children 1–2 years of age. ○ The Handbook also confirms that mouthing behaviors span more than one year of a child’s life. EPA should provide support for the assumption of only 250 total days of mouthing per child. • For the general population and consumers, EPA accounts for dermal exposures to dust, soil, and materials, and inhalation of suspended particles, but does not account for HBCD exposure that occurs from the air-to-dermal pathway in indoor environments. ○ Estimates based on established exposure models predict that the air-to-dermal pathway would contribute to a young child’s total residential exposures to HBCD. • EPA should consider the amount of HBCD that may remain in the air	In the revised assessment, EPA has used mouthing durations of 3 minutes/hour (central) or 9.7 minutes/hr (high end) for 13 hours a day (time spent awake), amounting to 39 to 126 minutes per day. The mouthing durations are based on the mean and 95th values in Exposure Factors Handbook for the sum of "all soft plastic item," "non-soft plastic toy, teether, and rattle," and "other item." The 13 hours was derived from CHAD data. In the revised assessment, EPA assumed an exposure frequency of 365 days per year for 1 year. See Section 2.4.4.4 for more details. Skin wipe data was used in the background exposure assessment, which accounts for air-to-dermal pathway. The current relative dermal contribution to the aggregate assessment is relatively low, and it appears that an assessment of the air to dermal pathway would not add appreciable risk. EPA considered aggregate background concentrations that may not be tied to a particular source but are expected to be inclusive of those listed in the comment. Additionally, a consumer scenario for building insulation was assessed. EPA did not provide distinct general population or consumer risk estimates for women of childbearing age but did include developmental endpoints and lifestages following acute exposure and additionally has

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	and on surfaces following home renovation or demolition projects, a source of potential inhalation, dermal, and oral exposures to residents, including children and pregnant women.
	
	• EPA should identify fetuses, infants, and young toddlers as a population with potentially greater exposure.
	  ○ EPA's analysis of human biomonitoring data shows that placental and fetal tissues have the highest measured doses of HBCD, falling outside EPA's estimated high-end doses range from exposure pathways, and infants and young toddlers have the greatest exposures compared to other age groups in the general population.
	  ○ HBCD is found in breastmilk.
	• In the risk evaluation, it was unclear if the exposure assessment fully considered children's exposure, even though child-specific exposure factors were used.
	• EPA presented, without comment, data showing that the fetal and placental exposures are much higher than other exposures (Figure 2-2) and did not consider higher infant exposures compared to mothers, as in the biomonitoring study by Kim and Oh (2014).
		clarified that thyroid chronic concerns are relevant to developmental concerns as well.
		
		Section 2.4.8 describes exposure PESS considerations. A subsection describes "exposure scenarios where greater exposure from multiple sources may occur and individuals who may have greater potential for exposure to HBCD", including a discussion of infant exposure via breastmilk and hand to mouth activity. Distinct exposures are estimated for all lifestages based on different activity patterns and exposure factors.
		
		Dietary exposure for infants (based on breastmilk consumption) is lower than for other age groups with no breastmilk consumption.
		
		EPA used the conservative assumption that the fetal exposure was equal to the mother's external exposure. It should be noted that the magnitude difference between the mother and infant (12 and 16 ng/g) was not nearly as great for HBCD as for the other chemical analyzed (TBBPA; 9 and 83 ng/g) and the author only discussed possible reasons for the difference for TBBPA.

54	**PUBLIC COMMENTS:** • EPA assumes that infants do not consume fish, but in fact, tribal infants do ingest fish during the infant stage, often with oral or manual softening preparation assistance.	EPA did not assess tribal populations quantitatively in this assessment due to too much uncertainty relating to variability among tribes and the location of tribal populations relative to potential sources of HBCD release. EPA assumes that the assessment of subsistence fishers is applicable most communities, however there is no reasonably available data for estimating infant fish ingestion. EPA provided risk estimates for aggregate exposure to infants assuming exposure beyond the 99.9%tile, with risks not identified.
Conditions of Use		
24, 57	**PUBLIC COMMENTS:**	EPA obtained and considered reasonably available

	• EPA must provide supporting evidence that uses have in fact ceased. o EPA did not survey all HBCD producers and users or use its information collection authorities under TSCA Sections 8 and 11 to independently confirm the lack of ongoing HBCD uses. ▪ Instead, EPA based the risk evaluation on voluntary and unverified reports from industry and its own research in public databases. o Industry's promises not to resume these uses are informal and unenforceable and do not provide assurance that they will not be revived in the future. o Uses were listed as "discontinued" in the risk evaluation without explanation. o Because the excluded uses of HBCD could return to the marketplace in the future if not restricted, EPA should account for their potential for exposure and risk in its HBCD evaluation. o It is reasonably foreseen that HBCD could again be used in the ways described. ▪ EPA must issue Significant New Use Rules ("SNUR") to ensure that the agency receives notice prior to any resumption of such uses.	information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation. EPA gathered information on the current use of HBCD from reliable government data sources (such as CDR, TRI) and interactions with industry associations and companies that have historically used HBCD. As discussed in Sections 1.22 and 1.23. of the RE, the reported production volume of HBCD is believed to be zero based on communications with major US manufacturers and all indications point to a dramatic reduction in the production and use of the chemical. Datamyne, a third-party data source, indicates that since late 2017 there has been no import of the chemical. Viable alternatives have already been adopted in the market, including Dow Chemical which has developed the polymeric flame retardant (Blue Edge) for use in insulation boards that is replacing HBCD. It is licensed to other manufacturers including Albemarle, Chemtura, and Bromine Compounds Limited (part of ICL Industrial Products; these companies sell the chemical under different trade names. However, EPA will continue to improve on its method and data collection for the next round of chemicals to be assessed under TSCA. The explanation for why EPA called some uses "discontinued" is contained in the problem formulation. However, the final risk evaluation does not exclude those uses. As noted in Section 1.2.9 of the risk evaluation, in developing the scope for HBCD, EPA learned that HBCD was no longer used in the processing of four minor-use products or articles: adhesives, coatings,

		high impact polystyrene (HIPS) in electronics, and textiles.[2] These "legacy uses" were excluded from the scope in the Problem Formulation along with related activities in later stages of the chemical life cycle, such as commercial/consumer use or disposal of HBCD-containing products and articles for which HBCD manufacture, processing and distribution for use in such products/articles has ceased (*Problem Formulation for Cyclic Aliphatic Bromides Cluster*, Section 1.2.7). EPA received public comments stating that the HBCD risk evaluation should include "legacy use." In 2019, the Ninth Circuit Court of Appeals ruled that EPA cannot categorically exclude "legacy use" and "associated disposal" from risk evaluations (*Safer Chemicals, Healthy Families v. U.S. Envtl. Prot. Agency*, 943 F.3d 397, 425 (9th Cir. 2019). Because of the court ruling in Safer Chemicals Healthy Families v. U.S. Envtl. Prot. Agency, EPA has added conditions of use for the activities it had excluded as "legacy uses" and "associated disposals" in the draft risk evaluation. The Agency added new conditions of use for the commercial/consumer use and disposal of products and articles that are no longer processed using HBCD. The four products and articles could still be in service, for example textiles containing HBCD used for seating in public buildings and conveyances, or electronics products or components in aircraft, office buildings, homes, or other indoor environments. Migration of the flame retardant from the products and articles can expose occupants to HBCD aerosols and particles in indoor air or dust.

[2] Available information indicates that only a small amount of HBCD was used for these and other minor products and articles. At least 95% of the total production volume was processed to manufacture XPS/EPS insulation, and only a single company was identified as having used HBCD in adhesives with the same being true of coatings. Use of HBCD to process consumer textiles had phased out by 2011.

		This comment is suggesting that the exposure/risk work develop hypothetical case studies. It is unlikely that discontinued products containing HBCD will re-enter the market because the manufacture, import, and use of HBCD has dramatically declined and is phasing out worldwide, including in the United States and major manufactures and importers have indicated no intention of returning to production of the chemical. A substitute chemical has replaced HBCD in its major use (insulation) and for discontinued uses, HBCD was presumably not essential. EPA acknowledges the suggestion that the Agency promulgate a Significant New Use Rule.
62	**PUBLIC COMMENTS:** • The "conditions of use" are the circumstances under which a chemical "is intended, known, or reasonably foreseen to be manufactured, processed, distributed in commerce, used, or disposed of." o Under the statutory definition of "conditions of use," the risks from use and disposal of HBCD require consideration independent of whether the chemical continues to be manufactured. o By separating the activities in that definition with the disjunctive "or," as opposed to the conjunctive "and," Congress requires EPA to evaluate each lifecycle stage of a chemical even if some of the chemical's lifecycle stages have been discontinued	For the final evaluation EPA has added two new conditions of use for minor-use products that it had considered "legacy use" and "associated disposal" respectively, in the draft risk evaluation. (Section 1.2.8). At the beginning of the Risk Evaluation process for HBCD, EPA had information that a small percentage of the chemical's production volume was used in several products and articles, including electronics. Further investigation led EPA to conclude that HBCD was no longer manufactured, processed, or distributed for use in such products and articles. The uses of HBCD in such products and articles and the disposal of those products and articles were therefore excluded from the evaluation as "legacy uses" and "associated disposal," respectively. In August 2019, EPA completed its draft Risk Evaluation on the narrowed scope, and later that year, the court made its ruling in Safer Chemicals Healthy Families v. U.S. Envtl. Prot. Agency. Because of the court ruling, as well as public and SACC review comments, EPA included "legacy" uses of HBCD in products in and articles, and disposal of those products and articles as conditions of use within the

		scope of this risk evaluation.
53	**<u>PUBLIC COMMENTS:</u>** • EPA must consider routes of exposure from consumer products, including through direct exposures, leaching into the household environment, leaching from food packing materials into food, and contamination of the marine food web. • EPA did not consider exposures that may occur through the presence of HBCD as a contaminant in consumer products. It is unclear how EPA can come to a conclusion about the level of risk from HBCD while eliminating potentially important sources of exposure (conditions of use) from consideration.	For direct exposure the EPA assessed children's mouthing of articles/products, insulation in home, and car consumer scenarios. EPA assessed dietary fish consumption for the general population, considering HBCD concentration in purchased fish for the general population. If HBCD was a contaminant in consumer products, the risk would be addressed by the assessment of background levels in indoor environments that is contained in the risk evaluation.

41	• EPA should take background exposures from legacy uses, associated disposal and legacy disposal of HBCD into consideration.
	  ○ EPA's decision to exclude legacy use and disposal, as a mandated condition of use by TSCA, from the risk evaluation disproportionately affects tribes' exposures.
	  ○ Little or no information is currently available to state and local jurisdictions related to disposal of HBCD-containing products.
	  ○ EPA could have developed this information by conducting an inventory of HBCD following recent guidance published by the United Nations Environment Program (UNEP).
	  ○ This would facilitate an effort to estimate the future exposure from legacy uses of HBCD and determine the optimal methods of recycling and disposal to prevent unreasonable risk to the humans and the environment.
		As stated in the draft risk evaluation, EPA initially decided to exclude legacy use and associated disposal for the first ten chemicals risk evaluations. However formerly termed legacy uses are now included in risk evaluations. For the final HBCD risk evaluation, EPA added and assessed a new condition of use for commercial/consumer use of minor-use products made with HBCD and a new condition of use for disposal of those products.
		
		The exemption at TSCA § 6(c)(2)(D)(i) refers to risk management rules, not to risk evaluations. EPA evaluated the risks from processing HBCD in the manufacture of replacement parts because of inconclusive data on whether the manufacture had stopped. EPA evaluated risks of automotive replacement parts, not production parts used in new vehicle assembly.

53 54	• EPA considers vehicle replacement parts to be a condition of use and includes replacement parts the scope of the HBCD risk evaluation. ○ Under TSCA § 6(c)(2)(D), the EPA is directed to "exempt replacement parts for complex durable goods and complex consumer goods" unless EPA finds that "such replacement parts contribute significantly to the risk, identified in a risk	

47	evaluation conducted under subsection (b)(4)(A), to the general population or to an identified potentially exposed or susceptible subpopulation." ○ Motor vehicle suppliers have indicated "HBCD is not used during the manufacturing process of any automotive components" and that industry has phased out the use of HBCD. ○ HBCD can only be found in vehicle replacement parts but is not currently used in production parts used in new vehicle assembly.	
Tiered Modeling Approach		
31, 51	**PUBLIC COMMENTS:** • Increased clarity is needed about how the Agency arrived at its overall approach to the environmental exposure assessment of HBCD, including more detail on the input parameters and assumptions contained in each model and including a flow chart describing how EPA utilizes both monitoring data and modelling data to inform a tiered approach to the assessment of HBCD. ○ EPA should include sensitivity analyses in its environmental exposure models where assumptions and significant uncertainty are prevalent. Sufficient information regarding the reason for the additional analyses, and the impact the analyses have on the risk characterization and ultimate risk determination, should be included in a clear and transparent manner. ○ Additional values of migration rates from insulation materials should be included in order to reduce uncertainty in inhalation estimates and increase confidence in the modeled levels. ○ Further discussion on the circumstances when the VVWM-PSC model will be employed and information about appropriate input parameters would be helpful. ○ EPA should also be clearer about the assumptions contained within each model because nested assumptions and uncertainties can lead the models to provide unrealistic exposure levels.	EPA added diagrams that represent the process for utilizing monitoring and modeled data, similar to those used at the SACC presentation. For the HBCD final risk evaluation, EPA performed two sensitivity analyses, varying HBCD half-lives and production volume for select exposure scenarios. The rationale for the sensitivity analysis for production volume is provided in Section 2.2.15. EPA selected two lower production volumes as a possibility existed that an unidentified site could manufacture or import at any volume below 100,000 lbs/yr. For this assessment E-FAST is a screening level tool that provides surface water concentrations regardless of fate properties *e.g.*, half-life, whereas the VVWM-PSC model does take these properties into account. The former model is a higher throughput, more conservative model than the latter model, which is why EPA prioritized only those scenarios that underwent E-FAST and exceeded the COC for lower throughput more conservative modeling. The models used in the exposure assessment are publicly available models and EPA provided

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	• Regarding sensitivity analysis, EPA should identify the question it is trying to answer and establish the criteria by which the sensitivity of the variables is assessed.
	• Reviewers agree with use of a tiered approach to derive exposure levels for the risk evaluation.
	  ○ At a screening-level, this approach allows EPA to quickly recognize conditions of use with potential unreasonable risk and identify any data needs prior to analysis using a higher-tier model.
	  ○ A tiered approach also provides a de-facto means to analyze sensitivity for a given exposure scenario by incorporating protective assumptions that are replaced with more accurate data in higher-tier models.
	• It is not clear why EPA used all of these approaches for analyzing and estimating environmental exposures, or how applicable this approach would be to risk evaluations of other chemicals.
	• EPA should include a flow chart describing how EPA utilizes both monitoring data and modelling data to inform a tiered approach to assessment, and going forward, develop a detailed program specific guidance.
		summaries and links to the model documentation, which features their default parameters and assumptions in Appendix F and Appendix G.
		
		The lack of additional values from migration rates may contribute to the uncertainty in the exposure estimates. However, these additional values may not necessarily change the overall low risk for the general population. Table 2-54 provides the inputs used in the VVWM-PSC tool. See Section 2.3.2.2.2 for additional information on inputs, outputs, which includes various assumptions and references.
		
		The purpose of the qualitative sensitivity analysis was to shed light on the potential uncertainty and variability from various assumptions and model inputs and that carry forward from chemistry, fate, and engineering releases through exposure, environmental and human health risks.
		
		EPA agrees with these comments: A tiered approach also provides de-facto means to analyze sensitivity for a given exposure scenario by incorporating protective assumptions that are replaced with more accurate data in higher-tier models.
		
		These approaches were relevant for persistent and bioaccumulative chemicals with multiple scenarios to be assessed along with various levels of modeling sensitivities, uncertainties, and receptors/endpoints, and throughput.
		
		EPA used only modeling data and not monitoring data to apply a tiered modeling approach. Diagrams have been added to the assessment that assist with describing the approaches such as Figure 2-2.

Environmental Hazard - Public and Peer Review Comments		
Charge Question 7.1: Please comment on the methodologies used to evaluate potential HBCD trophic transfer in aquatic and terrestrial ecosystems. **Charge Question 7.2:** What other information can be incorporated into the evaluation? **Charge Question 7.3:** Please comment on the use of mammalian studies, which were evaluated using human health metrics through the Systematic Review process, in the evaluation of HBCD risk to wildlife mammals.		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 7**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 7.1		
Additional discussion needed		
SACC	**SACC COMMENTS:** • Amphibians are an important interface between terrestrial and aquatic ecosystems. Amphibians are currently not mentioned in the Evaluation but should be discussed and justification for exclusion provided. (p. 129)	EPA systematically reviewed the reasonable available literature on environmental hazards of HBCD, including one reasonable available study on amphibians. This study conducted by Schriks, (2006), was not in the draft risk evaluation document that was submitted for review to the SACC peer review panel in July of 2019. Since then, the study has been summarized in the environmental hazard section of the document.
SACC	**SACC COMMENTS:** • Thyroid hormones are critical to an amphibian during thyroid hormone driven metamorphosis. HBCD has been shown to potentiate T-3-induced tail tip regression, the starting process of metamorphosis. The Committee recommended referring to the paper by Schriks et al., (2006). (p. 129)	EPA systematically reviewed the reasonable available literature on environmental hazards of HBCD, including one reasonable available study on amphibians. This study conducted by Schriks, (2006), was not in the draft risk evaluation document that was submitted for review to the SACC peer review panel in July of 2019. Since then, the study has been summarized in the environmental hazard section of the document.
SACC	**SACC COMMENTS:** • Sex-specific transfer of HBCD. In amphibian reproduction, fat is remobilized to be part of eggs. For instance, up to 23% of injected PCB126 can be transferred to eggs. This has gender-specific and trans-generational implication (Huang et al. 2000). HBCD is a lipophilic compound and may act like lipophilic planar PCBs. The Agency probably has limited information regarding amphibians. However, the Committee	Language was added to uncertainty section in environmental risk characterization to address the likelihood of HBCD exposure underestimation. HBCD has been measured in peregrine falcon and chicken upwards of 15,000 and 5,800 ng HBCD/g lw, respectively; (Guerra, 2012; Tao, 2016). In addition, HBCD has also been quantified in milk

	suggested that the Evaluation should discuss studies on fish and other aquatic or terrestrial species that can infer sex-specific transfer of HBCD to the offspring and its consequential effects. (p. 129)	from both humans and dairy cows (10 and 5.3 ng HBCD/g lw, respectively; Glynn, 2011; Shi, 2017). The presence of HBCD in the eggs of both aquatic and terrestrial birds, as well as the milk of terrestrial mammals, suggests that sex-specific transfer is an elimination pathway of HBCD for female birds and mammals that are reproductively active and resulting offspring are exposed to HBCD before and after birth. The risk evaluation acknowledges this uncertainty and it is likely that the current environmental risk evaluation underestimates organism exposure to HBCD. It is likely that the current environmental risk evaluation underestimates organism exposure to HBCD. See Section 4.3.1 for This possible underestimation would not affect the risk determinations because EPA has found unreasonable risk to the environment for each condition of use that results in release of HBCD to water.
Clarifications		
SACC	**SACC COMMENTS:** • Page 279, Table 3-1: The Evaluation should list test organism species, provide greater detail on the "population" endpoints considered, and resolve issues with units on the avian MOEJ 2009 study. The MOEJ 2009 study protocol reports dosing in ppm but Table 3-1 reports dosing in µg/L where one expects to see µg/kg-day or similar units. (p. 129)	The test organism species are summarized in EPA's "*Environmental Hazard Extended Data Extraction Supplemental Document for Cyclic Aliphatic Bromide Cluster (HBCD)*" supplemental document. EPA has updated the units to mg/kg-day for this study and has revised the summary.
SACC	**SACC COMMENTS:** • Page 283 suggests exposure is based on mixed diet, but usually mass/mass not mass/vol. Paper not available in the Agency's HERO literature database. (p. 129)	EPA has addressed this error. The appropriate HERO ID is assigned for this study and was updated in the environmental hazard section.
SACC	**SACC COMMENTS:** • Page 283 Crump et al., 2010: What is the exposure pathway (units mg/L; drinking water? What was the dose mg/kg-d?)? The Committee asked that EPA provide all toxicity information in terms of oral dose. The Committee asked that EPA provide all toxicity information in terms of	EPA has updated the summary of Crump et al., (2010) to clarify the dosing process. HBCD was injected into the air cell of chicken eggs prior to incubation to observe pipping success. All units were converted to mg/kg/day.

	oral dose; otherwise use the information only in a qualitative manner. (p. 129)	
SACC	**SACC COMMENTS:** • Page 287, Table 3-2 – About 32% of the kestrel's diets in trophic transfer analysis is assumed to be Peromyscus (deer mouse). The other 68% of its diet is not discussed. The Evaluation should be specific that the remainder of dietary items are assumed to be uncontaminated and highlight this as an uncertainty for wildlife receptors. (p. 129)	This uncertainty (potential underestimation of HBCD uptake via diet) is addressed in Section 3.1.7 of the risk evaluation.
SACC	**SACC COMMENTS:** • Page 290, Table 3-3 – The "Effect Concentration" reported in this table is not well defined, and it is unclear how the values reported would be used in assessing toxicity in birds and mammals. If these values are intended to be used as TRVs (*i.e.*, risk based media concentrations), they should be reported as oral units of exposure (mg/kg-d). Current values seem to require a PBPK model and estimated egg loadings to be useful. Values discussed in Section 3.1.6 make more sense. (p. 130)	Risk quotients (RQs) nor TRVs were not calculated for birds and mammals because an appropriate assessment factor could not be derived based on the data and there were not sufficient data to categorize HBCD exposure to organisms with accompanying hazard data resulting from HBCD exposure.
SACC	**SACC COMMENTS:** • Page 292, Table 3-5 – various concentrations are provided as concentrations of concern for birds and mammals, but it is not clear to what these concentrations refer. A column is needed to describe media and exposure regime or provide a TRV and the endpoint on which it is based. References should be included as in previous tables. (p. 130)	EPA has updated Section 3.1.5 and Table 3-5 to clarify the environmental concern levels. Units were clarified so the concentration media and exposure regimes are transparent. References for each of the hazard thresholds are also now included in Table 3-5.
SACC	**SACC COMMENTS:** • Page 340 – The Evaluation should be specific on the endpoint that defines impaired reproduction in the female American kestrel when exposed to 3.27 ng/g ww. Comparisons are difficult if not impossible when oral doses are not universally reported in mg/kg-d as is typical for reproductive toxicity studies. (p. 130)	The Marteinson et al., (2012) was incorrectly cited as the 3.27 ng/g ww refers to the concentration of HBCD measured in American kestrel eggs following an *in ovo* exposure (28-d embryonic period via maternal transfer). This study was removed from the final risk evaluation. The American kestrel study used to characterize the hazard threshold (reproductive toxicity: clutch size) in Table 3-5 is from the Fernie et al., 2011 study (LOAEL= 0.51 mg/kg bw).
SACC	**SACC COMMENTS:**	EPA has updated the significant figures presented in

	• Page 510-512, Tables G.3.1 and G3.2: In the KABAM output, the numbers of significant digits reported imply a false level of precision. Consider using two digits below the decimal for all values. (p. 130)	the tables that present KABAM outputs, per the SACC comment.
Panel Recommendations (within response text; contractor's paraphrased recommendation in Bold)		
SACC	**SACC COMMENTS:** • Models and methods used to estimate exposures and hazards to wildlife must be clear and well supported. In the Evaluation, exposures to birds and mammals are apparently based on actual, though limited environmental monitoring data. However, precise criteria and the use of models are not specifically delineated to understand whether oral dose is compared with oral dose estimates using assumptions modeled from environmental media concentrations or if environmental media concentrations are compared to modeled exposure assumptions to derive a media-screening level similarly to the process used by EPA in the development of EcoSoil Screening Levels. The Committee suggested that the EPA provide a transparent process (an algorithm) for estimating oral dose/exposures from media concentrations and provide the process used to develop toxicity reference values for mammals and birds. (p. 127)	Wildlife dietary exposures (via oral dose) were estimated using exposure factors presented in the U.S. EPA Wildlife Exposure Factors Handbook (U.S. EPA, 1993b). Toxicity reference values were not derived for mammals and birds because an appropriate assessment factor could not be derived based on available information. Media exposure was derived for fish and earthworms based on both environmental monitoring data and predicted surface water, sediment and soil concentrations.
SACC	**SACC COMMENTS:** • Explain process EPA used to choose toxicity benchmarks for wildlife. • Additionally, the process for choosing toxicity benchmarks for wildlife is not provided. [NOTE: bullets were added below; not from original text] ○ It appears that a critical study approach is based on the NOAEL; however, the basis for selecting the study is not provided. [See below for related recommendation] ○ It would also help to provide a scatter diagram to help reviewers see the spread of the toxicity endpoints to ascertain corroboration of the reported outcomes. (p. 127)	EPA has updated the environmental risk section to provide justification for the organisms used to set benchmark levels for wildlife exposure to HBCD. In Section 3.1.5 of the risk assessment document, EPA provided a rationale as to why the organisms were chosen to derive the environmental concern levels for HBCD to wildlife. Although a graphic representation could provide a visual distribution of HBCD's toxicity, it is not necessary for this evaluation. It should be noted that EPA has a supplemental document that summarizes the environmental toxicity of HBCD. In addition, the complete data set for HBCD is provided in EPA's "HBCD Ecotoxicity Data Extraction Table for TSCA Risk Evaluation."

SACC	**SACC COMMENTS:** • Consider using an evidence integration procedure to choose toxicity benchmarks for wildlife. • The Committee recommended not to necessarily use the most sensitive study, but to employ an evidence integration procedure where studies of highest quality and relevance are utilized and fit a benchmark dose to those data, if possible, to derive a Toxicity Reference Value (TRV) (as what is done for human health). (p. 127)	EPA implemented a tiered approach for choosing the appropriate species to represent the toxicity of HBCD to the aquatic and terrestrial environment. In Section 3.1.4, EPA discussed the weight of the scientific evidence for deriving the concentrations of concern values. Since all studies were rated as acceptable and of high quality, EPA used the study that was the most biological, physical/chemical and environmentally relevant. Conceptually TRVs are similar to the concentrations of concern used in the risk evaluation where an assessment or uncertainty factor is incorporated in deriving a hazard threshold to incorporate uncertainties (*e.g.,* field to laboratory extrapolations, using a proxy species). Currently EPA does not have enough information to incorporate such uncertainties for taxa with less toxicity data (*e.g.*, birds and non-human model mammalian species) for developing TRVs or COCs for non-aquatic species.
SACC	**SACC COMMENTS:** • Review inconsistencies in reporting exposure (concentration versus dose). o There are many examples where concentrations in exposure media are provided. Other cases report dose. These inconsistencies in reporting exposure increases the uncertainty of the Agency's assessment. (p. 127)	EPA has updated the environmental hazard assessment by eliminating the inconsistencies between reporting dose versus exposure.
SACC	**SACC COMMENTS:** • Review inconsistencies in units for toxicity data and normalize all units to mg/kg-d. o There are also many inconsistencies in units for toxicity data (ng/g-d, mg/kg-d). The Committee recommended these all be normalized to mg/kg-d. (p. 127)	EPA has updated the dose units to mg/kg/day.
SACC	**SACC COMMENTS:**	EPA has updated the discussion to describe the reproductive and developmental effects associated

	• Review inconsistencies in toxic endpoints. • Inconsistences also exist in the toxic endpoint being used. For example, from the Ema et al., 2008 study, it is not clear whether the thyroid or reproductive endpoint is being used. The latter would be more practical in terms of the potential for a population-level effect. (p. 127-128)	with T4 expression observed when rats were exposed to HBCD (Ema et al., 2008).
SACC	**SACC COMMENTS:** • Provide more explanation/justification for selection of endpoints for receptors. • The Committee recommended the Evaluation specifically acknowledge that selection of endpoints for receptors is critical and in many cases taxon specific. For example, in earthworms, based on Shi et al., 2018 (listed incorrectly as Shi et al., 2015 in the Evaluation), growth was not significantly reduced, but an upregulation of superoxide dismutase (SOD) and heat shock protein (Hsp70) gene expression was observed. This suggests that a longer exposure to HBCD may result in organism-level toxicological effects. The question of how much longer an exposure would be needed remains unanswered. • The Committee reiterated that relevance of a statistically significant finding is not equivalent to a biological significant finding. The Committee wondered if significant elevation in either of these two biomarkers (SOD or Hsp70) is sufficient to produce organism-level effects. Typically, without validation, biomarkers of exposure are not equivalent to adverse effects that are relevant to the organism or population. (p. 128)	EPA acknowledges that using a non-apical endpoint was not the most appropriate hazard threshold for evaluating risk to specific taxa or receptors, which is earthworms in this situation. EPA is no longer using the effects reported in Shi et al. (2015) to represent the hazard effects to earthworms. EPA has used the endpoints (*i.e.*, mortality, reproduction) supported by the study conducted by Aufderheide, (2003). EPA is no longer using the effects reported in Shi et al. (2015) to represent the hazard effects to earthworms. EPA will use the endpoints (*i.e.*, mortality, reproduction) supported by the study conducted by Aufderheide, (2003).
Summary of Peer Review Comments for Specific Issues Related to Charge Question 7.2		
SACC	**SACC COMMENTS:** • The Committee requested the Agency to be specific showing exposure calculations, toxicity dose/benchmark evaluation and how effects concentrations are compared to environmental concentrations. This can be done in two columns in a table also integrating other receptors. (p. 130)	In Section 3.1.5 of the risk assessment document, EPA provided a rationale as to why the organisms were chosen to derive the environmental concern levels for HBCD to wildlife. Although a graphic representation could provide a visual distribution of HBCD's toxicity, it is not necessary for this evaluation. It should be noted that EPA has a

		supplemental document that summarizes the environmental toxicity of HBCD. In addition, the complete data set for HBCD is provided in EPA's "HBCD Ecotoxicity Data Extraction Table for TSCA Risk Evaluation."
SACC	**SACC COMMENTS:** • Display derivation for TRVs, the endpoint on which they are based, and utilize diagrams (scatterplots) demonstrating variability for species within a class, when sufficient data exist to do so. (p. 130)	In Section 3.1.5 of the risk assessment document, EPA provided a rationale as to why the organisms were chosen to derive the environmental concern levels for HBCD to wildlife. Although a graphic representation could provide a visual distribution of HBCD's toxicity, it is not necessary for this evaluation. It should be noted that EPA has a supplemental document that summarizes the environmental toxicity of HBCD. In addition, the complete data set for HBCD is provided in EPA's "HBCD Ecotoxicity Data Extraction Table for TSCA Risk Evaluation." As mentioned above, EPA does not have enough information regarding non-aquatic organisms to derive TRVs or COCs.
SACC	**SACC COMMENTS:** • Consider including amphibian and reptilian receptors and address the uncertainties with doing so. (p. 130)	During the systematic review process, EPA was able to include one acceptable amphibian study to show the effects of HBCD on this receptor. This study conducted by Schriks, (2006), was not in the draft risk evaluation document that was submitted for review to the SACC peer review panel in July of 2019. Since then, the study has been summarized in the environmental hazard section of the document. The results of the systematic review process did not produce any acceptable toxicity studies for the reptilian receptor.
SACC	**SACC COMMENTS:** • Evaluate partially de-brominated HBCD degradation products that result from anaerobic sediment degradation. ○ The Evaluation notes that several partially de-brominated HBCD degradation products resulted from anaerobic sediment degradation. Fate and effects of these degradants merit investigation. Without	EPA cannot determine how rapidly these degradants may form and how much will be present at any particular time. Thus, the estimation of the environmental concentrations of the degradants for use in the Risk Evaluation would be highly uncertain. The potential presence of degradants is now

	corroborating data, such degradants cannot be assumed to be less toxic than HBCD. Further, if these transformation products are more bioavailable (and they are likely to be) then they may be more toxic than the parent HBCD. In terms of HBCD in wastewater sludges and degradation in soils, the data in Venkatesan and Halden (2014) should be considered. (p. 100).	acknowledged in the uncertainty sections of the risk evaluation.
SACC	**SACC COMMENTS:** • Follow-up on intermediate degradation products in terms of properties and toxicity is indicated. (p. 110)	EPA cannot determine how rapidly these degradants may form and how much will be present at any particular time. Thus, the estimation of the environmental concentrations of the degradants for use in the Risk Evaluation would be highly uncertain. The potential presence of degradants is now acknowledged in the uncertainty sections of the risk evaluation.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 7.3		
SACC	**SACC COMMENTS:** • Discuss how differences in gut physiology and trophic position can affect inferences on toxicity and exposure when extrapolating from one species to another species. • Because of the general lack of wildlife models for mammals and the abundance of rodent data for human health extrapolation, it is reasonable and not uncommon to use rodent data in assessing wildlife risks. However, the effects generally seen in syngeneic rodent models typically occur at lower exposures than those seen in wildlife species of the same taxonomic order. This logic can be used to support the decision to not use additional uncertainty factors to extrapolate to other species within the class. The rodent models typically used in toxicity studies and those used as receptors to make decisions are often sufficiently different physiologically to potentially affect kinetics from exposure. This is the case in this Evaluation, where rodents are being used to extrapolate to mustelids (otter; mink) and quail used to extrapolate to osprey or kestrels. Differences in how gut physiology and trophic position can affect inferences on toxicity and exposure should be discussed. (p. 131)	EPA acknowledges that gut physiology will likely impact HBCD exposure via trophic transfer. Section 4.3.1 within the risk evaluation has been updated to qualitatively discuss how gut physiology will impact HBCD uptake and depuration, and prey selection.
SACC	**SACC COMMENTS:** • Make correction to Table 4.2 regarding TRV for mammals.	TRVs were not calculated for birds and mammals because an appropriate assessment factor could not

	○ The study uses, as the TRV for mammals, a NOAEL for reproductive effects, not thyroid based as mentioned in Table 4.2. (p. 131)	be derived based on the available hazard data and there was not sufficient data to categorize HBCD exposure to organisms with accompanying hazard data resulting from HBCD exposure.
SACC	**SACC COMMENTS:** • Review exposure units reported from toxicity studies and present as mg/kg-d when possible. • Issues remain throughout the Evaluation where exposure units reported from toxicity studies are inconsistent with risk assessment requirements. As mentioned previously, units for exposure should be presented as mg/kg-d when possible. (p. 131)	EPA converted the exposure units that are inconsistent to mg/kg-d.
SACC	**SACC COMMENTS:** • Consider enhancing method for choosing a TRV. ○ The method for choosing a TRV may be enhanced by using benchmark dose analysis to develop a POD as a TRV. (p. 131)	EPA has updated Section 3.1.5 and Table 3-5 to clarify the environmental concern levels for aquatic organisms and terrestrial organisms. For aquatic organisms, the revised table will only summarize concentrations of concern values that were discussed in Section 3.1.5 and are summarized in Table 3-2. For terrestrial organisms, the revised table will only summarize environmental concern levels. EPA will consider methodologies for deriving TRVs in the future, should there be a enough information available to do so.
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 7**	**EPA/OPPT Response**
General		
62 62	**PUBLIC COMMENTS:** • The HBCD degradation product 1,5,9-cyclododecatriene is "highly toxic to aquatic organisms" and "may cause long-term adverse effects in the aquatic environment" as reported in five substantial risk reports. ○ This information should be presented in the draft risk evaluation. • EPA must evaluate the effects of dietary exposures to HBCD for invertebrate and fish species or increase the uncertainty factor used in its environmental risk evaluation to account for the absence of such information.	EPA acknowledges that HBCD has many degradation products, however EPA only evaluated the risk resulting from exposure to the parent compound. The risk evaluation acknowledges the formation of various HBCD degradation products however EPA did not characterize degradant-associated risk. EPA cannot determine how rapidly these degradants may form and how much will be present at any particular time. The potential presence

62 62	• EPA considers "only clearly adverse signs of toxicity," such as "lethality, immobility, effects on growth and reproduction, organ histopathology, [and] abnormal behavior," to determine toxicity effects levels for ecological receptors. o Developmental toxicity, embryo malformations, thyroid effects, oxidative damage, and others were not considered. o EPA's Guidelines for Ecological Risk Assessment specifically note that "adverse effects of a particular stressor may be important during one part of an organism's life cycle, such as early development," and recommend consideration of developmental effects. o EPA cites studies which were classified as "high quality" under its systematic review demonstrating HBCD's embryonic toxicity, developmental toxicity, and cardiac development effects in fish. ▪ However, the risk evaluation then states, that those studies "assessed endpoints beyond those evaluated in this assessment." ▪ The basis for the exclusion of these endpoints should be provided. • EPA should explain why it does not consider these endpoints, which are likely to be among the most sensitive, in the HBCD risk evaluation.	of degradants is now acknowledged in the uncertainty sections of the risk evaluation. Additionally, In vivo metabolism of HBCD varies by stereoisomer (Section 3.2.2.1.3) and the expected distribution of resulting products cannot be sufficiently quantified. Any toxicity from HBCD metabolites would likely be accounted for in long-term animal studies on the parent compound. The risk evaluation evaluates the effects of dietary exposure to HBCD for both aquatic and terrestrial organisms, when hazard information resulting from dietary exposures are available; hazard information for invertebrates and fish are not available for dietary exposures. EPA does not have an uncertainty factor that accounts for differences in exposure pathways (media vs. dietary), or varying sensitivities due to different exposure pathways, however EPA will include this consideration in the environmental hazard uncertainty discussion. EPA considered all hazard endpoint types when evaluating the environmental hazard of HBCD to aquatic and terrestrial organisms. Additional discussion to integrate all hazard endpoints was added.
62	**PUBLIC COMMENTS:** Other Potential Sources of HBCD Release into the Environment That Should Be Considered: • Degradation and transformation of HBCD in the environment. o EPA identified tetrabromocyclododecane, dibromocyclododecane, and 1,5,9-cyclododecatriene as degradation products of HBCD. o Given that EPA expects HBCD to degrade in sediment, these degradation products are likely to be present in the environment as a direct result of HBCD's conditions of use. ▪ EPA received five "substantial risk reports" for 1,5,9-cyclododecatriene under TSCA Section 8(e), indicating that the chemical is a possible reproductive toxin, a	EPA acknowledges that HBCD has many degradation products, however EPA only evaluated the risk resulting from exposure to the parent compound. The risk evaluation acknowledges the formation of various HBCD degradation products however EPA did not characterize degradant-associated risk. EPA cannot determine how rapidly these degradants may form and how much will be present at any particular time. The potential presence of degradants is now acknowledged in the uncertainty sections of the risk evaluation.

59	possible neurotoxin, and is "toxic to aquatic organisms" and "may cause long-term adverse effects in the aquatic environment. ▪ The Canadian government has found that some degradation products (*e.g.*, 1,5,9-cyclododecatriene) are potentially bioaccumulative. ▪ None of these findings are mentioned in the draft risk evaluation. ▪ EPA should evaluate the risks associated with these degradation chemicals. • EPA has failed to consider the risks posed by HBCD's degradation products and has adopted conflicting positions for 1,4-dioxane and HBCD. In the draft risk evaluation for 1,4-dioxane, EPA declined to consider the risks associated with the presence of 1,4-dioxane as a byproduct or impurity in consumer products, and stated that such risks are "better" addressed when EPA evaluates the chemicals that "generate 1,4-dioxane as an impurity or cause it to be present as a contaminant." In the draft risk evaluation for HBCD, EPA is evaluating the chemical that causes 1,5,9-cyclododecatriene to be present as a contaminant in sediment. EPA should explain why byproducts are better evaluated with the parent chemical, but degradation products are not. • EPA must include HBCD byproducts generated during the conditions of use in the evaluation of risk for HBCD.	Additionally, In vivo metabolism of HBCD varies by stereoisomer (Section 3.2.2.1.3) and the expected distribution of resulting products cannot be sufficiently quantified. Any toxicity from HBCD metabolites would likely be accounted for in long-term animal studies on the parent compound. The risk evaluation evaluates the effects of dietary exposure to HBCD for both aquatic and terrestrial organisms, when hazard information resulting from dietary exposures are available; hazard information for invertebrates and fish are not available for dietary exposures. EPA does not have an uncertainty factor that accounts for differences in exposure pathways (media vs. dietary), or varying sensitivities due to different exposure pathways, however EPA will include this consideration in the environmental hazard uncertainty discussion. EPA considered all hazard endpoint types when evaluating the environmental hazard of HBCD to aquatic and terrestrial organisms. Additional discussion to integrate all hazard endpoints was added. EPA cannot determine how rapidly these degradants may form and how much will be present at any particular time. The potential presence of degradants is now acknowledged in the uncertainty sections of the risk evaluation.
Species Selection		
62	**PUBLIC COMMENTS:** • EPA selected the American Kestrel as a proxy species for other avian species to evaluate trophic transfer and risks to birds. o Kestrel do not eat fish, and thus are not representative of the many aquatic bird species that do. o Since HBCD is primarily released to and accumulated in aquatic ecosystems, EPA's selection of Kestrel is likely to underestimate dietary exposures and risks to piscivorous bird species such as the	EPA acknowledges that the evaluation using American Kestrel only accounts for a limited portion of the American Kestrel's diet, therefore likely underestimating HBCD uptake. To account for this, EPA updated the HBCD trophic transfer discussion by adding an evaluation of a piscivorous bird (*i.e.*, osprey).

62 62	Kingfisher, Great Blue Heron and Osprey. ○ EPA should evaluate effects of HBCD on at least one of those piscivorous species in its final risk evaluation. • EPA selected Mink as a proxy for other mammal species. ○ Unlike Mink, Harbor Seals consume fish and partially inhabit both aquatic and land-based ecosystems, where they are preyed on by terrestrial predators. ○ Harbor Seals are better able to link the aquatic and terrestrial food webs and would have been a more appropriate choice of mammal species for analysis. ○ There are monitoring studies of HBCD concentrations in Harbor Seals, which EPA should have considered in evaluating risks to mammals. • The risk evaluation also underestimates risks to Kestrel and Mink (and thus to all species for which they serve as a proxy). ○ EPA is able to account for only 31% of the Kestrel's diet and 56% of the Mink's diet, then assumes no HBCD exposure from the remaining portions of their respective diets.	Mink was chosen as the representative terrestrial predator of aquatic prey (*i.e.*, fish), because HBCD trophic transfer is not limited to aquatic ecosystems; mink diet is characterized in the U.S. EPA Wildlife Exposure Factors Handbook, and therefore used to assess how 100% fish diet may result in HBCD uptake by a terrestrial organism that inhabits and consumes prey from aquatic ecosystems. The use of monitoring studies to characterize risk to Harbor Seals or other organisms that primarily consume fish and inhabit both aquatic and terrestrial ecosystems would still only provide exposure estimates; hazard and risk will still be difficult to characterize. There is limited hazard data for higher trophic level organisms, due to HBCD exposure. Specifically, there is no hazard data for higher trophic level aquatic organisms, or terrestrial organisms that inhabit and consume aquatic prey. EPA has already acknowledged in the uncertainty discussion that the evaluation likely underestimates kestrel and mink exposure to HBCD.
Other		
62	**<u>PUBLIC COMMENTS:</u>** • For Kestrels and Mink, EPA assumes there is no HBCD exposure from portions of the animals' diets that could not be accounted for. ○ Support for this assumption should be provided in the risk evaluation. EPA acknowledges that it "likely underestimates HBCD uptake" and understates the resulting risk.	EPA assumes that 100% of mink diet comes from higher trophic level fish, and therefore calculated mink HBCD exposure via diet accordingly. However, in regard to kestrels, EPA acknowledges that due to data gaps regarding kestrel exposure factors, there are limitations in the estimation of kestrel dietary HBCD exposure and that EPA likely underestimates HBCD exposure and risk for kestrels.

Human Health Hazard – Public and Peer Review Comments		
Charge Question 8.1: Please provide comment on whether there are other comparable high-quality studies that might be recommended for further consideration for dose-response for additional critical effects and for acute or chronic exposure scenario consideration. **Charge Question 8.2:** Please comment on EPA's justification in the document for consideration of developmental toxicity risks following acute exposures. **Charge Question 8.3:** Please comment on EPA's justification in the document for consideration of developmental toxicity risks in all age groups. **Charge Question 8.4:** Please comment on whether EPA should consider thyroid hormone effects as an acute endpoint. **Charge Question 8.5:** Please comment on EPA's justification and approach to modeling this chronic endpoint based on the data available in (Ema et al., 2008). **Charge Question 8.6:** Please comment on the evaluation of human health hazards and weight-of-evidence characterization. **Charge Question 8.7:** Are there any additional HBCD specific data and/or information that should be considered? **Charge Question 8.8:** Please comment on any other aspect of the human health hazard assessment that has not been mentioned above.		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 8**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.1		
SACC	**SACC COMMENTS:** • The Committee identified a recent study by Rasinger et al., (2018), not cited in the Evaluation, as one that merited additional review. In this study, low dose exposure to HBCD, CD-153 or TCDD induces histopathological and hormonal effects and changes in brain protein and gene expression in juvenile female BALB/c mice. In this study, exposure was to juvenile mice for 28 days of exposure to HBCD, concentrations that are considered relevant to human dietary exposure. While not a conventional developmental toxicity study, this study demonstrates effects from short-term HBCD exposure on a susceptible life stage and the Evaluation should discuss it. (p. 133)	EPA has added this study to the hazard ID and WOE sections where applicable. This study is not usable for dose-response based on the absence of clear identified adverse effect to correlate with histopathology findings and only one dose tested.
SACC	**SACC COMMENTS:** • Ema et al., (2008) reports on a two-generation reproduction study in Sprague-Dawley CD rats with HBCD given at 0, 150, 1500, and 15,000 ppm in diet. F0 and F1 follicle size decreased, and T4 was increased in F0	EPA performed BMD modeling on all effects from Ema et al., (2008). By using BMD modeling to model the dose equivalent to a predesignated benchmark response rate, the reported NOAEL or LOAEL of a study is not needed. Thus, the stated

	females at 1500 and 15,000 ppm; thyroid weight was reduced at these doses and liver weights increased. In F2 offspring, viability was reduced at 15,000 ppm. Body weight was initially increased then decreased in F1 progeny at 1500 and 15,000 ppm. There was delayed eye opening in the F1 at 1500 ppm (in males and females) but not at 15,000 ppm. In F2 offspring, eye opening was delayed in males and females at 1500 and 15,000 ppm. In addition, F1 male progeny had faster righting times, whereas females had longer times at 15,000 ppm. These opposite effects at the same dose are not likely to be reliable. No effects were found on 1-hour open-field activity. In the Biel water maze, 1500 and 15,000 ppm HBCD exposed males had shorter latencies, and at 15,000 ppm made fewer errors on the third test day (out of 3 days of testing when given 3 trials/day). • Ema et al., (2008) used multiple one-way ANOVAs done separately on males and females. A better approach would include a 'Dose x Sex' interaction term in a two-way ANOVA. This approach allows testing for a possible treatment 'x' sex interaction effect, and results in more sensitive statistical tests overall. The mid-dose female-only "air right effect" was not dose-dependent and unlikely to be reliable. Shorter Biel maze latencies and errors on day-3 of the test in the 15,000 ppm group may represent a sporadic effect and should not be relied upon. When behavioral data are dose-dependent, they are more credible. This is also the case if they occur in both sexes (although sex-specific effects are known for some compounds), and convergent across tests measuring related behaviors. This is not the case for effects reported in Ema et al., (2008). Moreover, shorter latencies and fewer errors in the Biel maze suggest improved learning, rather than impairment. However, notwithstanding these concerns, Ema et al., (2008) did find several effects in both the 1500 and 15,000 ppm HBCD groups, therefore, it is recommended that 1500 be used as the NOAEL. (p. 134)	NOAEL of the study was not used as a POD for the risk evaluation and is not mentioned in the risk evaluation.
SACC	**SACC COMMENTS:** • Van der Ven et al., (2009) used Wistar rats exposed to HBCD prior to mating and throughout gestation and lactation by dietary exposure to	EPA agrees with this assessment, and this study was not selected for use in dose-response analysis due to the availability of better studies with larger group

	doses resulting in exposures of approximately 0, 0.1, 0.3, 1, 3, 10, 30, and 100 mg/kg. They report finding markers of immunity changed and reduced testicular weight suggesting endocrine disruption. A limitation of the study is small group sizes. (pp. 134-135)	sizes.
SACC	**SACC COMMENTS:** • Lilienthal et al., (2009) use the same rats as van der Ven et al, (2009) and report changes in haloperidol induced catalepsy recovery and brainstem auditory evoked potentials. At HBCD exposures of 1 to 10 mg/kg the authors report shorter movement latencies after haloperidol in females but not males. They also report increased auditory evoked potential thresholds and longer early wave latencies at these same doses. The catalepsy test used 0.25 mg/kg of haloperidol with observations at 30 and 60 minutes after being placed in different positions and timing latency to move, but only 60-minute results are reported. Data are based on 5 males and 5 males per group from an unspecified number of litters plus additional females from other litters from the 0.3 mg/kg group, and additional rats from one other litter from the 20 mg/kg HBCD group. The authors report shorter movement latencies in the 30 and 100 mg/kg females. P-values are reported, not F-ratios or degrees of freedom (DF), making aspects of the analysis difficult to determine. For brainstem auditory evoked potentials, effects are reported in males using a benchmark analysis, although the ANOVA was (apparently) not statistically significant. Evoked potential thresholds are increased at 30 and 100 mg/kg HBCD based on a linear trend analysis. No pairwise comparisons between exposed groups and controls were conducted. The linear trend was heavily influenced by the highest dose group, and in some cases supported by data from the second highest group. It is unclear why these data are analyzed by trend analysis, when other data are analyzed by ANOVA. This study has methodological deficiencies, including small group sizes, no control for litter effects, and inconsistent and poorly explained statistical methods. The Committee indicated EPA should not rely on this study for neuro effects. (p. 135)	EPA agrees with the committee and this study was not considered for dose-response analysis due to the issues stated.
SACC	**SACC COMMENTS:** • Genskow et al., (2015) tested HBCD in cell culture in SK-N-SH cells (a catecholaminergic cell line). HBCD at up to 25 micro-molar	This study was mentioned in the risk evaluation, however there was no significant effect on actual dopamine concentrations so the importance of this

	concentrations for 24 hours caused cell death. In primary neuronal culture HBCD reduced growth and survival of tyrosine hydroxylate-positive cells at 72 hours at concentrations up to 10 micromolar. In C57BL/6J mice, gavaged with 25 mg/kg/day HBCD dissolved in corn oil for 30 consecutive days and striatum analyzed 24 hours after the last dose, found significantly reduced DAT (dopamine transporter) and VMAT2 (vesicular monoamine transporter-2) where found by western blot with no change in tyrosine hydroxylate protein expression. It was not clear to the Committee why the in vivo data from this study is not used in the Evaluation and a justification for this exclusion is needed. (p. 136)	study is muted. This data has been more explicitly highlighted in the neurological effects hazard ID section.
SACC	**SACC COMMENTS:** • The Evaluation reported on six epidemiological studies that examine associations between HBCD exposure and endpoints related to effects on thyroid, nervous system, and the male reproductive system. The Evaluation concludes that the epidemiological database is insufficient for dose-response assessment. The limitations of studies in experimental animals is thoughtfully described and the Agency concludes that two studies could be used for dose-response assessment (Ema et al., 2008, WIL Research 2001). As noted in the response to previous Questions, there is vagueness and potential inconsistency with how qualitative statements as "High," "Medium," and "Low" are used in the assessment of studies. Their meaning is not entirely clear in all cases and should be clarified. (p. 136)	High, Medium, and Low represent the resulting score ranges from the data quality evaluation of each study. In the majority of cases these are determined by the quantitative metric score, however they may be adjusted based on expert judgment.
SACC	**SACC COMMENTS:** • The WIL Research (2001) study is available in the Agency HERO database, but the study's peer review status was unclear. At the meeting of the committee, EPA clarified that this study was reviewed by Agency staff and found acceptable. This should be noted in the Evaluation along with a description of how the review was performed. (p. 136)	The High evaluation score indicates that it was reviewed and scored of high quality.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.2		
SACC	**SACC COMMENTS:** • One of the outcomes in the Ema et al., (2008) study is loss of litters. The Evaluation combines the litters lost data from two generations within the	This endpoint was removed from dose-response analysis. EPA acknowledges that it is not suitable for combining and there is no statistically significant effect reported in the study for a NOAEL to be used

	study in its analysis. When combined, a significant HBCD effect is obtained. The Committee expressed concern over how these data are combined and an alternate approach was suggested. One Committee member suggested that at a minimum the analysis model should estimate a generation effect (one degree of freedom) prior to examining the HBCD dose-response effect. The decision to combine data requires more justification. (p. 137)	in lieu of a BMDL.
SACC	**SACC COMMENTS:** • The definition of what is an adult human use in the Evaluation seems to be different than that used in cited articles. The Evaluation uses as cutoff ages of 16 or 21 years whereas most literature uses 18 years of age as the first adult age group. Justification of the different threshold age for an adult is required. Consideration should be given to standardizing the first adult age as 18 years. (p. 137)	The distinctions among age groups listed in the Risk Evaluation are based on different exposure factors used for exposure dose estimation as cited from EPA's 2011 Exposure Factors Handbook (ex: adult workers use values for 21+ years old, while female workers use values for 16-50 years old). These distinctions were not limiting when assessing potential developmental hazards to any of these groups.
SACC	**SACC COMMENTS:** • The Committee discussed, in the context of developmental effects, the extent to which the same MOA could be used for both humans and rodents. How rodent data is used to extrapolate to humans requires more discussion and more justification on why rodent developmental endpoints chosen are relevant to humans. (p. 137)	Additional discussion was added to the WOE section describing that increased sensitivity of rodents may only be true for adults but developing rodents and humans can be reasonably expected to be similarly sensitive.
SACC	**SACC COMMENTS:** • The Committee recognized the significance of the identified thyroid effects from HBCD exposure, but also noted significant uncertainty around the different thyroid endpoints. The Committee expressed that the Evaluation did not discuss the range of this uncertainty adequately. (p. 137)	Additional language has also been added to the uncertainty section to discuss issues about the relevance of thyroid effects to humans. Additionally, substantial discussion has been added to the thyroid effects WOE, Section 3.2.4.1.1.
SACC	**SACC COMMENTS:** • The Committee suggested that justification for not considering a developmental MOA for liver effects be included in the Evaluation. (p. 137)	Liver effects as observed in adult rodents would not be expected to have any differential developmental effect in offspring compared to adults.

SACC	**SACC COMMENTS:** • The Evaluation notes that effects were found on the thymus. The Evaluation should discuss how thymus effects have the potential to cause significant effects, including long-term effects, on the immune system. (p. 137)	The reference to potential long-term immune system effects from thymus effects has been added to the hazard ID section, however this does not alter the WOE for immune system effects.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.3		
SACC	**SACC COMMENTS:** • The Evaluation notes that developmental effects would not be expected to manifest at younger life stages (page 365). The fact that HBCD does bioaccumulate means that early life exposure could result in later-life effects. Nevertheless, the Committee was not certain that these conclusions are self-evident and thus requires more discussion in the Evaluation. (p. 138)	That section additionally discusses that developmental effects were observed in neonates that were developmentally exposed. In the absence of adequate reasonably available studies on younger lifestages, it cannot be ruled out that exposure during childhood could result in some of these developmental effects.
SACC	**SACC COMMENTS:** • The Evaluation is not clear on how the multi-generational bioaccumulation of HBCD, as noted by Ema et al., (2008), works given that this was a continuous, two-generation feeding study in which the body burden of HBCD may increase with each generation. The use of multigenerational effects is reasonable, likely due to the accumulation and persistence of HBCD. While using such data is reasonable, it may be an overly conservative approach. One Committee member believed this to be justified due to the severity of some of the observed effects. (p. 138)	EPA agrees that applying developmental outcomes from an F2 population to acute exposures is conservative and health protective, however the persistence of HBCD within human tissues suggests that even an acute external exposure results in a long-term internal dose. Therefore, the assumption of developmental outcomes following acute exposure is reasonable.
SACC	**SACC COMMENTS:** • On Page 313: "From a statistical standpoint, most reproductive and developmental studies with nested study designs typically support a BMR of 5% extra risk (ER) (U.S. EPA, 2012). A BMR of 1% ER was used in this case to address the severity of this endpoint (*i.e.*, offspring loss), in accordance with EPA Benchmark Dose Guidance (U.S. EPA, 2012), which supports use of smaller BMRs for more severe or "frank" effects." Considering some of the uncertainties in the database, the Committee questioned whether the use of a smaller BMR is justified. Perhaps more explanation would help support this choice. (p. 138)	A 1% BMR is typically used for mortality or endpoints resulting in potential mortality, since any incidence of mortality would be considered an unreasonable risk for any percentage of the population. This statement has been added to the risk evaluation. BMR selection is based on endpoint severity and not endpoint uncertainty, unless there are substantial concerns about the range or model fit of the data. EPA also disagrees that there are substantial uncertainties about the developmental hazard database.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.4		

SACC	**SACC COMMENTS:** • Page 299: "In humans, (Eggesbø et al., 2011) reported elevated but non-statistically significant odds ratios for increased thyroid stimulating hormone (TSH) in relation to increased HBCD levels in human breast milk, but confidence intervals (CIs) around point estimates were wide and a dose-response was not observed." If the odds ratio change is not statistically significant, the Evaluation should report this as a no effect finding rather than imply inconclusive evidence. (p. 139)	This has been corrected as suggested (Section 3.2.3.1.1).
SACC	**SACC COMMENTS:** • Page 304: "Additionally, a review of the hypothalamic-pituitary-thyroid (HPT) axis across species published more recently than the NAS review (Zoeller et al., 2007) states that there is minimal evidence linking biochemical and metabolic differences in thyroid hormones (due primarily to reduced serum binding proteins in rodents) to differences in sensitivity among rodents and humans except on a MOA-specific basis." This statement is unclear and seems to imply a different MOA may be responsible for effects in humans compared to effects in rodents. (p. 139)	Context has been added clarifying that the risk evaluation focuses on developmental effects during gestation following changes in adults, and that developmental effects are expected to be comparable between rodents and humans. The uncertainties section has also been expanded.
SACC	**SACC COMMENTS:** • Page 304: "Therefore, overall the weight-of-evidence indicates that rodents are an adequate model for assessment of thyroid disruption by HBCD, however it is possible that quantitative extrapolation may overestimate the adversity of effects in humans." No evidence is presented to support the adequacy of rodents for this response. Significant questions are raised that are not addressed, primarily because few experimental data address this question. Developmental exposure also led to alterations in thyroid hormones in both sexes and across studies of different exposure durations. This is notable given female rats are considered less sensitive to thyroid effects than male rats (Choksi, et al., 2003). However, it is not clear that the concentrations of HBCD that generated these changes are relevant to human exposures and further discussion is needed on this issue. (p. 139)	Additional detail has been included which clarifies that while there is some uncertainty whether adult rodent data may overestimate quantitative responses in humans, the data does not suggest that developmental exposures are likely to significantly differ between rodents and humans. Therefore, the effect on thyroid hormones has been framed in more of a developmental context, and the changes in thyroid hormones serve as an early biochemical marker of downstream developmental neurotoxicity, which EPA was unable to assess quantitatively via dose-response analysis. Therefore, the POD for developmental thyroid hormone changes can be seen as a surrogate for developmental neurotoxicity.
SACC	**SACC COMMENTS:** • The evidence supporting the proposed MOA for thyroid seems weak and	See above.

	non-specific. The Evaluation seems to down weight the differential role of thyroid hormone glucuronidation in humans versus rodents (noted on page 304). The existence of inconsistencies in the literature and the poorly characterized interspecies differences regarding MOA, adds uncertainty to the use of thyroid effects as an acute exposure endpoint. Better justification for the use of thyroid effects is needed and the Evaluation should clearly state the limitations with using thyroid effects. (p. 139)	
SACC	**SACC COMMENTS:** • The Committee discussed the potential for hormone effects, including those related to thyroid hormones, to display a non-monotonic (either U-shaped and inverted U-shaped) dose-response form. Such non-monotonic responses have been documented for exposures to endocrine disrupting chemicals, which may include HBCD. The Committee suggested that the Evaluation might wish to discuss this possibility. (pp. 139-140)	It is unclear how this possibility has an influence on the dose-response assessment of the risk evaluation, which used BMD modeling to find the best model fit to the data and would have considered any non-monotonic dose-response.
SACC	**SACC COMMENTS:** • Saegusa et al., (2009) and WIL Research (2001) reported follicular cell hypertrophy as a result of exposure to HBCD. The Committee suggested that further clarification is needed in the Evaluation as to whether this effect is adverse or recoverable. (p. 140)	Follicular cell hypertrophy was not identified as the most sensitive thyroid effect compared to T4 hormone reduction. The adversity and quantifiability of the effect were part of the consideration in not using it for dose-response. A result can be not statistically significant despite a large effect due to high variability among samples resulting in large standard error. These considerations and others are explained in the Supplemental Human Health Hazard document.
SACC	**SACC COMMENTS:** • WIL Research (2001) reports effects at 1000 mg/kg, but these effects are reported as not significant (NS) with reductions of greater than 20%. This finding requires further discussion. (p. 140)	It is unclear what endpoint the commenter is referring to; however, a large effect may still not be statistically significant if there is large variance in the measurements (*i.e.*, large standard deviation)
SACC	**SACC COMMENTS:** • Additional acute or short-term studies on thyroid hormone effects should be included in assessing human health hazards. The Committee provided two reasons for asking for these studies: a) lipophilic chemicals that possess some chemical properties that are similar to those of HBCD have	There are no reasonably available short-term thyroid studies on HBCD. Some short-term studies are already mentioned for other thyroid disruptors. Rawn (2014b) just indicates HBCD biomonitoring,

	been found to be thyroid disruptors in laboratory animals, and b) perturbation of thyroid hormones by PCBs, PCDDs, and PCDFs have been identified in field species such as birds, amphibians, and other terrestrial mammalian species in acute or short-term studies. (p. 140)	and it is already known that HBCD crosses the placenta. This study was cited in the TK section and was added to the PESS section.
SACC	**SACC COMMENTS:** • In the study by Ema et al., (2008) the increased incidence of non-pregnancy in HBCD-exposed F0 or F1 rats alone is not statistically significant with either a pairwise test (as reported by authors) or the Cochran-Armitage trend test (as conducted by EPA). Dose-response curves were shallow and never reached a high response percentage. The results of several statistical tests indicate that F0 and F1 datasets are compatible for combining. Therefore, the Evaluation reported this change to be biologically relevant and a log-logistic model fit to the combined response data (which only demonstrated adequate fit after dropping the highest dose) was used to derive the BMDL for this chronic endpoint. In a previous Question, the Committee recommended the Evaluation revisit this model fit and account better for potential F0 and F1 differences. (p. 140)	This POD has been removed for these reasons.
SACC	**SACC COMMENTS:** • The Committee discussed the available information on thyroid markers but was divided on the utility of these data as surrogates for adverse health effects. More information and more study are needed to demonstrate that changes in thyroid markers translates to changes in health. (p. 140)	From Section 3.2.5.2.2: Specifically, adequate levels of T4 are necessary for normal growth and development, and altered thyroid homeostasis has the potential to affect numerous organ systems, including neuronal, reproductive, hepatic, and immune systems (Forhead and Fowden, 2014; Gilbert and Zoeller, 2010; Hulbert, 2000). The following has been added from the supplemental human health hazard document into Section 3.2.5.2.2: Reductions in maternal T4 during pregnancy or the early postnatal period are strongly associated with adverse neurological outcomes in offspring. In humans, mild to moderate maternal thyroid insufficiency is associated with higher risk for persistent cognitive and behavioral deficits in children.

Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.5		
SACC	**SACC COMMENTS:** • The weight-of-evidence characterization of the four health effect domains (thyroid, liver, female reproductive and developmental toxicity), the acute and chronic exposure effects, and the use of rodents to model of HBCD thyroid effects seem appropriate, if conservative, given the available literature. However, better documentation of the HBCD concentration information associated with these studies in the Evaluation would make it easier for readers to assess how the same endpoints are likely to be altered by human exposure. (p. 141)	The dose range for each study is listed in Section 3.2.5.2 for selection of studies for dose-response and derivation of PODs.
SACC	**SACC COMMENTS:** • The Evaluation needs to better justify why the 1500 ppm LOAEL from Ema et al., (2008) is not used in the risk assessment. (p. 141)	PODs from Ema et al., (2008) are all based on BMDL modeling, which incorporates all dose-response information from the study. This adds refinement beyond use of simple NOAELs or LOAELs.
SACC	**SACC COMMENTS:** • Page 303: "A pattern of increased TSH, a sensitive early indicator of decreased thyroid hormone reserve…" One Committee member suggested prefacing this statement with: "Increased TSH is a sensitive early indicator of disruption of the thyroid hormone economy, including decreased thyroid hormone synthesis or secretion, decreased serum concentrations of T4, or decreased deiodination of T4 to T3 in peripheral tissues." The phrase "a sensitive early indicator of decreased thyroid hormone reserve" can then be dropped. (p. 141)	This has been done as recommended.
SACC	**SACC COMMENTS:** • Page 303: "A few studies demonstrate that HBCD may induce human health hazards downstream of thyroid hormone dysregulation through activation of the DNA-binding thyroid receptor." The Evaluation should provide more detail on what expected downstream effects of activation of the thyroid hormone receptor might be. It is possible that activation of the thyroid receptor could reduce TSH secretion from pituitary thyrotropes. (p. 141)	The downstream effects of thyroid hormone receptor activation would be the same as are described in the assessment, namely dysregulation of neuronal, reproductive, developmental, hepatic, and immune systems. The supplemental human health document provides more detail covering downstream effects such as morphological development and cell proliferation. These two outcomes have been added to the body text for additional context.
SACC	**SACC COMMENTS:** • Page 315: "Although the adversity of increased liver weight was	It has been clarified that liver weight is a good quantitative marker when associated with other

	ambiguous in some studies, it serves as an effective and sensitive toxicological indicator for liver toxicity, especially within a susceptible population. Increased liver weight was therefore selected as the representative endpoint for dose-response analysis of liver effects based on being the most consistently observed toxicological effect." The characteristics of "ambiguity" and "sensitivity" appear contradictory. The Committee recommended that this statement be modified to clarify the contradiction, restate the weight of the scientific evidence argument for liver weight as the appropriate toxicity endpoint, and remove the suggestion of subjectivity in choice of adverse effects for the risk assessment. (p. 141)	effects.
SACC	**SACC COMMENTS:** • Page 317: The Evaluation provides a rationale for using a 5% ER rather than a 10% ER for assessing risk for female reproductive toxicity and pregnancy incidence. The justification for this is unclear and creates a sense of bias. Using a smaller BMR for developmental effects because of severity of endpoint seems contrived. This discussion should be reviewed and revised to improve the justification and remove the suggestion of bias in ER selection. (p. 141)	Use of a smaller BMR for more severe effects is justified as described in EPA's Benchmark Dose Guidance. For more severe effects, the risk becomes unreasonable at a lower percentage of affected population.
SACC	**SACC COMMENTS:** • Page 319: The Committee discussed the rationale given in the Evaluation for employing an interspecies uncertainty factor (UFA) of 3. The Committee suggested using the default of 10 can be better justified in this case. (p. 141-142)	Allometric scaling accounts for interspecies toxicokinetic differences. Therefore, only an UFA of 3 remains to account for toxicodynamic differences. The toxicokinetic differences are accounted for in derivation of the Human Equivalent Dose (HED).
Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.6		
Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.7		
SACC	**SACC COMMENTS:** • The Evaluation should make clear those endpoints that have been identified but deemed not amenable to quantitative risk analysis. When data on these endpoints are available, justifications for exclusion of these endpoints from the risk assessment should be clearly stated. (p. 142)	EPA explicitly states in Section 3.2.4.1.5 through 3.2.4.1.8 of the Risk Evaluation that these hazards were not carried forward for dose-response analysis. Any details not provided in the Risk Evaluation body text can be found in the supplemental document, *Supplemental Information on Human Health Hazard*.
SACC	**SACC COMMENTS:**	A statement has been added to this effect in Section

	• The summary of liver effects (Section 3.2.4.1.2) in the Evaluation is adequate but does not discuss that exposure to HBCD may have additive or synergistic effects when combined with a high fat diet. Also, for liver effects, there is no discussion on potential modes of action (MOA). There are numerous studies which could be useful in identifying potential liver MOAs. (p. 142)	3.2.4.1.2.
SACC	**SACC COMMENTS:** • There is no discussion of dose-response relationships with human health effects in general or specifically in case of liver effects. (p. 142) • There are six studies considered for the liver effects, but only one is used for POD analysis. One study (van Der Ven et al., 2006) which includes the highest dose groups is not used, without adequate justification. The Committee concluded that this is an acceptable study, with 7 doses, BMD calculations and analysis in multiple organs. Justification for giving it no weight in the final analysis should be provided. (p. 142-143)	Section 3.2.5.2 has an explicit discussion of the process for deriving PODs from dose-response information. The van Der Ven study is considered in Section 3.2.5.2.2. It is excluded from considerations for dose-response because responses were not observed as consistently or in parallel with other markers of liver toxicity compared to WIL Research, (2001).
SACC	**SACC COMMENTS:** • Page 305: The location of the Wheater and Burkit (1996) reference suggests it provides mechanistic information on HBCD-induced liver lipid transport changes. This citation is a book chapter discussing basic histopathology. Its inclusion here should be justified. (p. 142)	This citation was a mistake and has been removed/replaced with other references.
SACC	**SACC COMMENTS:** • Information on Absorption, Distribution, Metabolism, and Excretion (ADME) is typically found in the body of a risk assessment not relegated to an appendix as is done in this Evaluation. The text provided in Appendix H is better suited to Section 3.2.2 Toxicokinetics. In reading the document, reviewers had to go back and forth between the main document and Appendix H. Neither discussion is comprehensive, but by merging Appendix H back into Section 3.2.2, the information flow is better than before, and redundancy is minimized. (p. 142)	This has been done, and the information from Appendix H has been folded into Section 3.2.2 .
Summary of Peer Review Comments for Specific Issues Related to Charge Question 8.8		
SACC	**SACC COMMENTS:**	Details on HBCD concentrations in toxicological

	• Information in Section 3.2.4 describing the studies used to assess the Non-Cancer Hazards of HBCD does not specify HBCD concentrations, making it difficult to estimate the relevance to human exposures. (p. 97)	assays are provided in Section 3.2.5 for those studies considered for dose-response analysis.
SACC	**SACC COMMENTS:** • On page 300, the two epidemiological studies (Roze et al., 2009, Kiciński et al., 2012) that did not find consistent nervous system effects following developmental exposure to HBCD are not referenced, unlike the rodent studies that did find neurological effects. More information regarding the human studies is very important in order to appreciate the relevance of the rodent studies. (p. 97)	The results of the studies were referenced however the studies were not cited themselves and limited details were given. Details from the WOE section on these studies have been incorporated into the hazard ID section.
SACC	**SACC COMMENTS:** • The results of the same animal studies are discussed more than once, which led to some confusion. For example, the thyroid effects of HBCD on rodents are discussed on page 299 in Section 3.2.1 Non-Cancer Hazard section, and again on page 302 in Section 3.2.4 Weight of Evidence (WOE). The same is true for other parameters. It is not clear whether this duplication is a requirement of the risk evaluation framework or a result of the document outline that discusses WOE after identification of available data. (p. 97)	EPA is maintaining the current format for the Final Risk Evaluation in order to remain consistent with all other First 10 chemical evaluations. However, EPA acknowledges this comment and will consider changes to the document format for future evaluations.
#	**Summary of Public Comments for Specific Issues Related to Charge Question 8**	**EPA/OPPT Response**
General		
31, 51	**PUBLIC COMMENTS:** • Several endpoints (thyroid, liver, reproductive, developmental – acute and chronic) are carried forward to dose response and are described as relevant based on the types of exposures expected from the conditions of use (CoU). Does the SACC agree with EPA's assessment of these endpoints?	EPA incorporated SACC comments on these endpoints into the final version of the HBCD risk evaluation. No major changes were made to the overall endpoints selected for dose-response.
Susceptibility		
59	**PUBLIC COMMENTS:** • EPA states that "The results of the available human health data for all routes of exposure evaluated (*i.e.*, oral, dermal, and inhalation) indicate that there is no evidence of increased susceptibility for any single group relative to the general population." However:	EPA agrees that this statement is inaccurate and has deleted it. EPA does not only evaluate women of reproductive

	○ EPA identified developmental and reproductive toxicity and effects on thyroid as key HBCD toxicity endpoints. ○ EPA acknowledges that "Thyroid hormones play a critical role in coordinating complex developmental processes, and perturbations of thyroid hormone levels in a pregnant woman or neonate can have persistent adverse health effects for the child… early development remains a sensitive life stage for hormone deficits, largely due to minimal reserve capacity when compared to adults. Effects on female reproduction parameters are an additional consideration for identifying pregnant and lactating females as a susceptible subpopulation." ○ Early life stages (fetuses, children) should have been evaluated as susceptible subpopulations. Abundant literature has identified critical windows of susceptibility during early life stages and pregnancy.	age quantitatively. EPA provides general population and consumer risk estimates for all life stages including the most susceptible via each exposure pathway. Additionally, EPA has added maternal thyroid hormone changes as an acute endpoint. Differences in dose among sexes and life stages are based on differences in intake rate (breathing, drinking, eating), surface area, and body weight, and this was the basis of the 10% difference for women of reproductive age. The Occupational Risk Calculator provides all these values for comparison. The HBCD draft risk evaluation did assess aggregate general population exposures to HBCD, with exposures from various exposure routes added together. This has been made more apparent in the final Risk Evaluation throughout the document, and a more thorough discussion of considerations for aggregate exposure was added to Section 4.4.2. Additionally, risk estimates for subsistence fishers have been added to the final version of the risk evaluation. Aggregate exposure was applied for the general population and consumers, incorporating background aggregate exposures for all exposure routes combined with specific modeled exposures for the pathway of interest. See additional details and considerations in Section 4.4.2.
59	• Risks of concern for 'highly exposed populations' for developmental toxicity after acute exposures related to fish ingestion were found. EPA recognizes that people with pre-existing health conditions or genetic pre-dispositions in any of the affected health domains "would also be expected to be especially susceptible to HBCD toxicity, perhaps at significantly lower doses than healthy populations." (This includes people with liver or thyroid disease).	
59	• EPA notes that because HBCD is bioaccumulative, both people that consume a high-fat diet and people with higher body fat content may have greater susceptibility.	
59	• Only one identified sensitive subpopulation (female workers of reproductive age) was addressed quantitatively. EPA states "Risk estimates for female workers of reproductive age were 10% lower than workers overall…" EPA should clarify how this 10% difference was derived.	
54	• Fish consumption is listed as the exposure route expected to be "the largest contributor to overall dose." EPA modeled wild fish exposure and upper trophic level fish concentrations to evaluate acute exposure. However, subsistence users were not evaluated as a sensitive, highly exposed population.	
53	• EPA should evaluate aggregate exposures to HBCD in the above sensitive populations.	

Developmental Toxicity		
62 53, 30, 56, 59, 6	**PUBLIC COMMENTS:** • The draft risk evaluation acknowledges the existence of "evidence to support HBCD-mediated neurotoxicity following developmental exposure." However, EPA chose not to quantify developmental neurotoxicity risks, citing "inconsistencies and/or limitations with the database." o EPA had previously assigned HBCD a "high hazard" designation for developmental neurotoxicity. o If such data require clarification or supplementation, EPA has authority to order additional testing (such as NTP's modified one generation study with a developmental neurotoxicity testing arm) under TSCA Section 4.91. o Neglecting to exercise that authority cannot be used as justification for failing to evaluate risks to pregnant women and children. • EPA failed to further assess or quantify developmental neurotoxicity results despite: o Evidence from animal studies indicating HBCD is a developmental neurotoxicant. o Specifically, HBCD has been associated with changes in rat thyroid systems and neurotoxic effects such as decreased fine manipulative abilities and lower attention in children. It is reasonable to assume HBCD disrupts brain development. o Prenatal exposure to HBCD may lead to subtle behavioral changes in rodents, particularly motor activity and cognition are affected (Eriksson et al., 2006). o Neuroscience research has identified "critical windows of vulnerability" during fetal development and early childhood, when the brain is especially at risk from toxic chemicals, even at extremely low exposure levels. o EPA considers the thyroid a sensitive organ for HBCD effects, and normal levels of thyroid hormones during pregnancy are critical to the baby's healthy brain development. o Infants and young toddlers have the highest exposures to HBCD compared to other age groups in the general population. o Placental and fetal tissues showed the highest doses of HBCD compared to all other populations. o HBCD is detected in the umbilical cord and breast milk.	In the absence of a study examining developmental neurotoxicity containing adequate dose-response information, EPA has added a POD for acute thyroid hormone changes to serve as a surrogate because thyroid hormones changes are an early molecular event leading to downstream effects on neurological development. Additionally, the application of acute exposures to the developmental endpoints is a conservative assumption that is also expected to be protective of neurological outcomes. EPA evaluated acute exposures for all COUs for occupational, general population, and consumers. EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to complete the HBCD risk evaluation using a weight of the scientific evidence approach in light of the limited time available under the statute for completing the risk evaluation. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation.

	○ EPA's exposure analysis finds that dust and diet are the major sources of HBCD exposure for infants and young toddlers. • EPA must consider acute exposures when evaluating developmental effects. • EPA should use its authorities to order developmental neurotoxicity studies to fill critical data gaps.	
Thyroid Hormone Effects		
31, 51 31, 51	**PUBLIC COMMENTS:** • Additional data should be considered for the evaluation of the thyroid endpoint in the HBCD final risk evaluation. • EPA states that "although the human evidence was inconclusive, oral toxicity studies in rodents provide evidence that HBCD exposure can result in dose-related perturbations of thyroid function." ○ EPA should consider information relevant to the potential for rat studies to overestimate the risks of enhanced thyroid hormone metabolism and clearance. ○ There are several factors that limit the impact of UGT T4(T3)-glucuronidation in humans. ○ A high affinity serum binding protein in humans, thyroid hormone binding globulin (TBG), binds approximately 80% of T4, limiting the amount of free T4 available for glucuronidation. In contrast, adult rodents express very low levels of TBG. Instead, rodents rely on lower affinity transport proteins that have faster dissociation rates for thyroid hormone, making thyroid hormone more readily available for metabolism and clearance. This is demonstrated by the shorter half-life of T4 and T3 in rats (0.5-1 day and 0.25 day, respectively) than humans (5-9 days and 1 day, respectively). ○ Fetuses and newborns have slightly different half-life for T4 relative to adults; however, their T4 half-life (3-4 days) is still considerably longer than rats. ○ There are species differences in enzyme regulation in rats versus humans, including both qualitative and quantitative differences in the activation of nuclear receptors and induction of phase I and II metabolism. ▪ PXR has low concordance in the ligand binding domain	EPA has added additional discussion clarifying that while rodent studies may quantitatively overestimate the effect of HBCD exposure on thyroid hormone changes, evidence does not support significant differences between rodents and humans for developmental HBCD exposure. Therefore, the rodent thyroid hormone data is being considered primarily in a developmental context. The following text has been added to the thyroid weight of the scientific evidence discussion which highlights the reviewer's points but clarifies the sensitivity of rats as a model for developmental thyroid effects: Biochemical and metabolic differences among adult rodents and humans may result in quantitative differences in dose-response and downstream outcomes as a result of decreased serum hormones levels. Thyroid hormone levels have much shorter half-lives in adult rats compared to humans, potentially due to a lack of high-affinity T4 binding proteins (*e.g.*, thyroxine-binding globulin, TBG), possibly making T4 more susceptible to removal (Zoeller et al., 2007; Choksi et al., 2003). Importantly, TBG is expressed in neonatal rodents and only decreases following weaning. TBG

31, 51	between humans and mice (77%), which markedly affects the response of this pathway to different xenobiotics across species (*e.g.*, pregnenolone-16α-carbonitrile is a highly effective ligand in rats whereas rifampicin is effective in humans). ▪ T3 and T4 are metabolized by different UGT isozymes in rats and humans, and compared to rodents, humans rely considerably less on glucuronidation for metabolism of both T4 and T3, preferring deiodination and sulfation. ▪ In contrast to rats, human SULT1A1 is not regulated by nuclear receptors. ▪ In vitro data also support differences in enzyme pathway induction between species; glucuronidation in rat primary sandwich culture hepatocytes (SCH) was 15-20x higher across all doses of PCB 153 (0.3, 3 and 30 μM) than human SCH, whereas sulfation and deiodination were greater in human SCH. • The design of rodent toxicity studies favors overestimation of the risks of enhanced thyroid hormone metabolism and clearance as these studies require exposure to maximum tolerated dose levels, which induce enzymes to cope with repeated, high-dose exposures to test compound. This may not occur in humans exposed to lower doses and slower dose rates. o These data should be considered in EPA's risk evaluation of HBCD.	increases during pregnancy in both rats and humans, while only in mice does TBG decrease throughout pregnancy (Choksi et al., 2003). In general, there are significantly fewer differences in thyroid hormone regulation between rodents and humans during development. In humans, mild to moderate maternal thyroid insufficiency is associated with higher risk for persistent cognitive and behavioral deficits in children (Finken et al., 2013; Julvez et al., 2013a; Román et al., 2013; Henrichs et al., 2010; Haddow et al., 1999). Similar effects have been described in animal studies, with modest reductions in maternal T4 during gestation resulting in behavioral alterations, learning deficits, and neuroanatomical changes in offspring (Gilbert et al., 2014; Gilbert et al., 2013; Gilbert, 2011; Liu et al., 2010; Ausó et al., 2004). Therefore, developmental effects of thyroid disruptors following gestational exposure are expected to be highly comparable between rats and humans, with substantially increased susceptibility in developing individuals of both species compared to adults. Additionally, because thyroid development proceeds later in rats than humans, human offspring may be susceptible *in utero* to many developmental outcomes that were observed only postnatally in rats (*e.g.*, mortality, reduced body weight). In contrast, humans exposed only neonatally may have developed compensatory mechanisms that are not yet fully formed in newborn rodents." The study used for thyroid dose-response was a 2-generation chronic study in which overt clinical signs of toxicity were only indicated slightly in the highest of three dose groups. PODs were determined from BMD modeling the dose-response at all doses, and for a bioaccumulative compound administered multi-generationally any metabolic responses would be expected to equilibrate.

Environmental Risk Characterization - Public and Peer Review Comments		
Charge Question 9.1: Please comment on the appropriateness of EPA's selections for deriving RQs. **Charge Question 9.2:** Please comment on the appropriateness of using this methodology for characterizing risk.		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 9**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 9		
Additional analyses needed		
SACC	**SACC COMMENTS:** • Critical body burden analyses should be carried out with PBT compounds such as HBCD. (p. 146) • Considering HBCD is a PBT, the Committee thought that E-FAST and KABAM models can be linked and used to predict critical body-burden tissue levels in fish, and these values can be divided by HBCD PNECs for fish health (4 mg/kg) (Arnot et al., 2009; European Center for Ecotoxicology and Toxicology of Chemicals (ECETOC), 2011). Methods for using critical body burdens in risk assessments can be found at ECETOC, (2011). (p. 145)	Per the recommendation to consider fish exposure to HBCD and resulting environmental risk, EPA has updated the hazard thresholds for aquatic organisms to include an acute concentration of concern (COC) based on a fish embryo exposure to HBCD. Using PSC-predicted surface water HBCD concentrations, risk to fish was calculated. Fish body burdens were also evaluated using BCFs to calculate HBCD uptake.
SACC	**SACC COMMENTS:** Risk characterization for birds should be included with discussions of uncertainty between fish consuming birds relative to non-fish consuming birds. (p. 146) The Committee expressed concern that fish-eating birds are not considered in the assessment of avian receptors. Kestrel data are not used to assess impacts in fish-eating birds because kestrels do not consume fish. Concentrations of HBCD in seabirds are at levels similar to those found in kestrels that cause reproductive impairment (AMAP 2017, Guigueno and Fernie 2017). If the seabird HBCD tissue residue data are consistent with that seen in wild falcons and in the reproduction toxicity study with kestrels, then it can be concluded the reproduction toxicity seen in the controlled HBCD feeding study will predict effects to seabird raptors. The AMAP (2017) lists several seabird species. The Committee concluded that Kestrel data can be used to assess seabird body burden, but with some uncertainty. (p. 145)	EPA acknowledges that fish-consuming birds may be exposed to HBCD at concentrations where reproductive effects have been observed in non-fish-consuming birds (*i.e.*, Kestrel). Therefore, EPA has updated the environmental trophic transfer of HBCD discussion to include allometric scaling for Osprey, using Kestrel reproductive toxicity data. EPA acknowledges the inability for the risk evaluation to account for a majority of American kestrel diet due to data limitations regarding the availability of monitoring data for kestrel prey. This uncertainty is further explained in Section 3.1.7 regarding the underestimation of organism uptake of HBCD via estimations using exposure factors and

	• Page 340: "Table 3-2 suggests that American kestrel are exposed to 64.4 ng HBCD per day through the consumption of small mammals (*i.e.*, mice), however mice only comprise approximately a third of American kestrel diet; it is likely that these calculations vastly underestimate HBCD uptake through diet." One Committee member observed that field data for birds of prey suggest high tissue concentrations occur occasionally for unknown reasons, thus demonstrating underlying uncertainty in relation to routes of exposure. (p. 146)	available monitoring data.
SACC	**SACC COMMENTS:** • Probabilistic assessments of Predicted Environmental Concentration (PEC) of HBCD should be included with discussions of uncertainty. (p. 146)	Uncertainties regarding environmental exposure parameters regarding both predicted and measured media concentrations have been included in Section 2.3.7.
SACC	**SACC COMMENTS:** • Hazard assessments should use thresholds that evaluate endpoints of growth, survival and reproduction (not biomarkers of oxidative stress as used in soil organisms). (p. 146) • The threshold concentration established for soil may not be relevant. To assess risk in soil, a 200 mg/kg threshold for worm toxicity is used in the RQ. A change in superoxide dismutase and HSP70 is used as an endpoint for toxicity. In the absence of validation and verification, use of biochemical sublethal endpoints is highly uncertain. Some Committee members thought these endpoints could be used in a screening capacity. However, if the accuracy of true exposure and bioaccumulation/biomagnification are low, then the estimation of risk in the face of inadequate data on toxicological consequences is suspect and can increase uncertainty. It is recommended that apical endpoints of survival, growth or reproduction be used for hazard threshold derivation. A Predicted No Effect Concentration (PNEC) of 59 mg/kg is suggested by Arnot et al., 2009. (pp. 144-145)	EPA will no longer use the adverse effects reported in Shi et al. (2015) to represent the hazard effects to earthworms. EPA will use the endpoints (*i.e.*, survival, reproduction) supported by a study conducted by Aufderheide (2003). This is the study that is referenced in Arnot et al., (2009). After closely reviewing the panel's recommendation, EPA will not apply the suggested environmental concern value (*i.e.*, PNEC) of 59 mg/kg to derive EPA's risk for soil organisms for the following reasons: First, the PNEC value that was reported in Arnot et al., (2009) is 5.9 mg/kg dry soil instead of 59 mg/kg dry soil. This value was derived from a NOEC of 59 mg/kg dry soil after normalizing for the actual content of HBCD in soil based on the European Union Test Guideline Document (TGD) (Volume #2). Also, Arnot et al., (2009), is an updated evaluation to the 2008 EU risk assessment report. In addition, the EU risk assessment applied an assessment factor of 10 to derive a PNEC value of 5.9 mg/kg dry soil. The rationale for this assessment factor for this analysis was not provided in the EU assessment. In

		establishing an environmental concern level for aquatic and terrestrial species, EPA has provided adequate protocol that supports EPA's rationale to deriving this value. For aquatic hazard, EPA uses concentrations of concern (COC) and the documentation for deriving the COCs are referenced in Section 3.1.5 of the risk assessment document. The COC values for acute fish and daphnia are derived by applying an assessment factor of 5. For chronic fish and invertebrates, an assessment factor of 10 is applied. For algae, an assessment factor of ten is applied. EPA has not derived an assessment factor for terrestrial organisms. Currently, the environmental risk for terrestrial organisms are established by applying the hazard value for soil invertebrates and wildlife using the risk quotient method. The rationale for deriving the risk for terrestrial organism has been revised and is provided in Sections 3.1 and 4.1of the risk assessment document. After further evaluation of the reasonably available acceptable data from the systematic review process, EPA has updated the environmental hazard and risk sections to include a different hazard effect threshold for earthworms for evaluating the risk of HBCD exposer to soil invertebrates.
Panel Recommendations		
SACC	**SACC COMMENTS:** • Address uncertainties discussed under Charge Question**.** o Using estimated water, sediment and soil concentrations, appropriate risk quotients (RQs) are made using thresholds and safety factors from the literature for these media. Acute and chronic toxicity thresholds are appropriate for plants, invertebrates and vertebrates for water, sediment and soil media. However, there are uncertainties, and these are primarily discussed in Question 7. (p. 144)	EPA recognizes that there are various sources of uncertainties due to the use of multiple streams of data used to characterize environmental exposure, hazard and risk. The RQs derived using monitoring data represent measured background exposures to HBCD, whereas RQs derived from predicted modeled data represent potential HBCD releases (exposure) from specific exposure scenarios and conditions of use. The uncertainties are addressed throughout the risk evaluation, and those relevant for environmental

		risk are addressed in Section 4.3.1.
SACC	**SACC COMMENTS:** • The Evaluation should include a rationale and justification for using the 50th percentile for biota concentrations from the Kow Based Aquatic Bio Accumulation Model (KABAM) (page 341) to characterize the exposure in fish tissues. It was unclear why a more probabilistic approach with Monte Carlo analyses was not used for the exposure assessment. A 90th percentile could also be used for comparison to the 50th percentile. While it is clear the Evaluation uses a 90th percentile in river water dilution models, an additional 90th percentile should be included in the overall predicted environmental concentration assessment. (p. 144)	EPA has updated the environmental risk section to predict exposure to HBCD in surface water and sediment using both high tendency (10^{th} percentile) and central tendency (50^{th} percentile) estimates for evaluating risk to aquatic organisms.
SACC	**SACC COMMENTS:** • Reconsider approach to evaluating food webs. ○ In general, the Committee expressed concerns over estimating water or sediment concentrations and then using those estimates to calculate bioaccumulation in food webs. Furthermore, dietary compositions of the predators in those webs are often not adequately understood. (p. 145)	The uncertainties regarding the use of either modeling or measured surface water or sediment HBCD concentrations to calculate bioaccumulation in food webs are discussed in Section 4.3.1. EPA used this methodology to provide exposure scenario-specific predictions for HBCD trophic transfer.
SACC	**SACC COMMENTS:** • Page 329: "Specifically, environmental monitoring data cannot provide HBCD release information that can be attributed to a specific COU or COU-specific parameter, nor can it be used to determine HBCD releases from a specific time period." Some Committee members suggested that passive sampling for waterborne hydrophobic contaminants can be conducted relatively inexpensively. The Committee also thought that the presence of HBCD within plastics/fragments is a major factor affecting HBCD fate and bioavailability but is not discussed adequately in the document. (p. 145)	Leaching of HBCD from landfills is discussed in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle. Specifically, EPA has considered the concentrations of HBCD reported in landfill leachate particulates from the Netherlands cited in the EU 2008 report. The values cited by the commenter were measured concentrations in leachate from two of nine landfills studied (de Boer et al., 2002). The range of concentrations in landfill leachate particulates from the seven other landfills sampled were approximately two orders of magnitude lower than those cited by the commenter. EPA discusses studies demonstrating the presence of HBCD in landfill leachate and provides rationale for why the leachate exposure pathway was not quantitively assessed in Section 2.4.5.2 HBCD Sent to Landfill Across the Lifecycle. Leaching of HBCD from microplastics has been

		added to the uncertainty section for environmental risk.
SACC	**SACC COMMENTS:** • On page 330: "There are many potential sources of uncertainty in all of the parameters involved in environmental exposure estimates. the greatest influence on exposure estimates given the associated uncertainty and sensitivity (effect on the final values) stems from the selection of emission factor and days of release. EPA believes that these sub-scenarios sufficiently capture the range of risk estimates for all reasonably expected environmental exposures, with minimal remaining unaccounted-for uncertainty. Therefore, EPA has high confidence in the range of risk estimates for the highly exposed aquatic and terrestrial organisms." With these uncertainties, knowing little about behavior of microplastics or the HBCD therein and the uncertainties regarding the role of discarded polystyrene debris, some of the Committee disagreed that categorizing risk estimates as "high confidence" is merited. The Committee suggested comparing model estimates for HBCD levels in Canadian falcons. The Committee indicated similar tissue concentration anomalies in terrestrial birds of prey for Decabromodiphenyl ether (DecaBDE), an extremely hydrophobic brominated flame-retardant additive that does not appear to substantially accumulate in fish (Potter et al., 2009). (p. 145)	EPA acknowledges that there may be sources of HBCD that are not accounted for in the risk evaluation (*e.g.*, leaching from microplastics or landfills) and has qualitatively discussed these uncertainties in Sections 2.4.5.2 and 4.3.1. Data limitations regarding the quantification and attribution of HBCD concentrations from sources or products not affiliated with an exposure scenario or condition of use does not allow for the quantification of environmental risk for these potential HBCD sources. EPA has high confidence that the environmental risk evaluation quantifies environmental risk using the best available science for aquatic and terrestrial organisms despite the many sources and types of uncertainties regarding the characterization of environmental hazard, exposure and risk resulting from HBCD releases. Furthermore, the inability to quantify spatially- and temporally related trends regarding HBCD releases and exposure may explain why birds of prey have varying body burdens of HBCD. This uncertainty is addressed in Section 4.3.1. Additionally, tissue concentration differences between aquatic and terrestrial organisms was expanded upon in Section 3.1.7, using the Potter et al., 2009 reference.
SACC	**SACC COMMENTS:** • Reconsider use of Great Lakes sites for "Near General Population" in Table 4-3 ○ Page 334, Table 4.3: The "Near General Population" sites are from the Great Lakes. One Committee member expected substantial dilution in the Great Lakes versus living just downstream of a WWTP, suggesting that the risk characterization may be less protective than indicated. (p. 145-146)	EPA has updated the environmental monitoring data used to characterize surface water HBCD concentrations. The mean and 90th percentile surface water concentrations used to derive environmental risk are now based on studies where HBCD water concentrations were measured from both lakes and rivers in different geographical regions.
SACC	**SACC COMMENTS:** • Reconsider threshold in Table 4-6 ○ Page 337, Table 4-6: The Committee expressed concern that the	EPA has updated the environmental hazard and risk section to reflect a different hazard effect threshold

#	Summary of Peer Review Comments	EPA/OPPT Response
	threshold of 200,000 µg/kg was chosen based on very limited data. (p. 146)	for earthworms for evaluating soil exposure to HBCD. EPA will no longer use the effects reported in Shi et al., (2015) to represent the hazard effects to earthworms. EPA will use the endpoints (*i.e.*, survival, reproduction) supported by the study conducted by Aufderheide, (2003).
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 9**	**EPA/OPPT Response**
General		

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	PUBLIC COMMENTS:
	• EPA found no unreasonable risk of injury to the environment under all conditions of use within the scope of the risk evaluation.
	    ○ Nearly every governmental and inter-governmental analysis of HBCD has found the chemical to be highly toxic to aquatic and terrestrial species. This is the conclusion of analyses by the United Nations Environment Program, the European Union, Environment Canada, Australia's National Industrial Chemicals Notification and Assessment Scheme ("NICNAS"), and EPA itself in its proposed listing of HBCD on the Toxics Release Inventory.
	    ○ EPA, however, concludes that HBCD presents no unreasonable environmental risks.
	    ○ If this determination is allowed to stand, the US will not restrict manufacture, processing, use and disposal of HBCD under TSCA.
	    ○ EPA may have based its determination of no unreasonable risk in part on the cessation of manufacturing and importation of the chemical in large quantities, and that it would be cost prohibitive to produce HBCD in small quantities.
	        ▪ Further explanation for this decision is required.
	• EPA acknowledges the contributions to exposure from construction and demolition debris, reuse, and other activities.
	    ○ It is unclear how EPA has concluded that there is no environmental risk from these sources.
	• All of the environmental risks presented by HBCD through ambient water should be evaluated.
		The result of new analysis of environmental risk following publication of the draft Risk Evaluation is that EPA found unreasonable risk for some of the conditions of use. These determinations are contained in Section 5 of the final risk determination.
		EPA acknowledges that a conclusion of no unreasonable risk would preclude action under TSCA Section 6(a).
		
		EPA also acknowledges that the commenter recommends more explanation of the risk determination conclusions.
		
		The HBCD Risk Evaluation draft considered HBCD use both in installation and demolition of building materials. The final risk evaluation has added environmental releases stemming from demolition, while estimated releases from installation have increased compared to the draft risk evaluation.
		
		The current risk evaluation does take into account consideration exposure to ambient water by using environmental monitoring data in its evaluation of risks from background levels of HBCD. The environmental risk uncertainty section has been updated to reflect additional factors that contribute to

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24, 57
 	
31, 45, 51
 	
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	• EPA should consider exposures and hazards to all aquatic organisms, including marine mammals.
	• It is noted that HBCD is a persistent, bioaccumulative, and toxic (PBT) compound that will persist in the environment, a reason to be more cautious rather than less cautious.
	• HBCD is bioaccumulative and the draft evaluation has not adequately captured the cumulative risks to the environment from long-term buildup of HBCD.
	• Throughout the document, EPA cites that there is no evidence that domestic manufacturing or import of HBCD is occurring, and that the estimates used for volume introduce significant uncertainty that may overestimate risk.
	  ○ Any conflict with the quantitative environmental risk characterization in the risk determination section must be very clearly addressed and explained.
	• In calculating risks to invertebrates and fish, EPA looks only at exposures from surface water and sediment; dietary exposures were not evaluated.
	  ○ There is evidence that fish readily accumulate HBCD via their diet.
	  ○ EPA must either evaluate the effects of dietary exposures to HBCD for invertebrate and fish species or increase the uncertainty factor used in its environmental risk evaluation to account for the absence of such information.
		possible over- or underestimations of HBCD exposure, uptake and environmental risk (*i.e.*, HBCD half-life, diet composition and variability, gut physiology, media and diet HBCD uptake). Specifically, HBCD half-life was further evaluated in the final risk evaluation to determine whether the use of HBCD half-lives of 11- and 128-days was sufficient; additional HBCD half-lives were used to predict surface water and sediment concentrations resulting from exposure-specific releases.
		
		EPA does consider exposure and hazard to all aquatic organisms. Reasonably available information used to assess environmental exposure and hazard are available in supplemental materials for aquatic organisms. Marine mammal exposure data is available in the supplemental materials (biomonitoring data), however there is a data gap regarding hazard data.
		
		EPA quantifies HBCD bioaccumulation for aquatic and terrestrial ecosystems in the Environmental Hazard section, by using multiple methodologies (Section 3.1.3). Uncertainties regarding the over- or under-estimation of HBCD bioaccumulation are addressed in Section 3.1.7.
		
		EPA addressed the uncertainty of not explicitly quantifying dietary HBCD uptake for invertebrates and fish.

RQs		
50 50	**<u>PUBLIC COMMENTS:</u>** • EPA attempted to characterize the environmental risk for HBCD by calculating risk quotients (RQ). An RQ equal to 1 indicates that the exposures are the same as the concentration that causes effects when considering appropriate uncertainty factors. If the RQ exceeds 1, the exposure is greater than the effect concentration and there is potential for	EPA acknowledges the commenter's description of how risk quotients are derived and the draft risk determination of no unreasonable risk (commenter's disagreement with the determination). EPA recognizes that using the predicted 50th percentile surface water and sediment HBCD concentrations

62 50 62 62 50, 62 62	risk presumed. For HBCD, the Agency determined that the RQ is 5.03 more than five times the environment risk driver benchmark. • The RQ calculations were then disregarded and a determination of no unreasonable environmental risk was made. EPA explained that a RQ of 1 was not a bright line test and that other risk-based factors may be considered. EPA should provide additional detail regarding the other risk-based factors that informed its finding of no unreasonable risk. • EPA has previously found that RQs of 1.49 "may present an unreasonable risk of injury" under TSCA's new chemicals program. • Some rationale for the conclusion of "no unreasonable risk" was provided in Table 5-1 and included: o EPA's assertion that its risk evaluation methodology was too conservative. ▪ EPA attributed the full amount of HBCD in a water body to each potential condition of use because EPA does not know how much each individual condition of use contributed to the contaminant load. This approach, however, does not make the risk evaluation overly conservative or less reliable. What matters is how high HBCD burdens are in recipient ecosystem water, sediment, fish, and other animals, not how it got there. • The monitoring data were collected at a time (5- 10 years ago) when the use of HBCD was produced in much higher volumes. ▪ If EPA believed that newer monitoring data were needed, it could have ordered the generation of such data under TSCA Section 4.74. ▪ Having chosen not to do so, EPA cannot discount the actual data in its possession. • EPA should use 10th percentile 7Q10 stream flow values instead of 50th percentile values. o EPA's Sustainable Futures guidance recommends the use of 10th percentile 7Q10 values, or the rate at which only 10% of emitting facilities would be expected to discharge to water bodies with a lower or equal 7Q10 flow. o Use of 50th percentile values overestimates stream flow rates and understates HBCD risks. o EPA's own sensitivity analysis found for virtually every condition	may underestimate exposure for aquatic organisms, and therefore included risk estimates derived using the 10th percentile surface water and sediment HBCD concentrations. EPA also has updated the environmental risk characterization section to include environmental risk conclusions. The addition of the 10th percentile flow assessment resulted in higher risk estimates and EPA has found unreasonable risk for some of the conditions of use of HBCD. EPA appreciates the comment regarding the interpretation of the environmental risk quantification and evaluation. The risk quotient calculations for environmental risk that are specific to exposure scenarios considered for each condition of use were not disregarded to determine whether there is environmental risk. The risk determination is based on the risk quotient calculations but also on uncertainties that could overestimate risk, including production volume and other factors listed in the comment (outdated monitoring data, etc.). Details of the risk-based factors are in Section 4.3.1. EPA has updated the environmental risk to include estimates based on the modeled 10th percentile surface water and sediment HBCD concentrations, resulting in additional exposure scenarios that may have environmental risk. EPA considers multiple routes of evidence when determining risk and unreasonable risk under TSCA. As such, different sections of TSCA that implement different programs (New Chemicals and Existing Chemicals), have different requirements regarding data source, quality, and evaluation. EPA appreciates the comment regarding the use of

	of use; risk quotients are at least 10 times higher using the 10th percentile values; many are more than 100 times higher (than when using 50% values).	the terminology "conservative," and has updated text that insinuates the methodology is too conservative, to clarify the use of "conservative" as a way of describing and comparing methodologies used to evaluate hazard and risk. EPA does not discount any data that has come through the systematic review process but weighs the data's relevance and quality. EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to complete the HBCD risk evaluation using a weight of the scientific evidence approach in light of the limited time available under the statute for completing the risk evaluation. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation.
62	**PUBLIC COMMENTS:** • For some species, EPA used modeling to estimate exposures in the absence of monitoring data. EPA warns that such modeling "incorporates several assumptions that could overestimate exposures." o EPA should detail the model assumptions that may overestimate exposure. o EPA should also identify assumptions (such as stream flow) that may underestimate exposure and risk. o EPA chose to rely on these models and their underlying assumptions, instead of collecting additional data or adjusting the models. • EPA should have determined, consistent with its calculated risk	EPA does not discount any data that has come through the systematic review process but weighs the data's relevance and quality. EPA did not use its TSCA data collection authorities to gather additional information for this chemical because EPA believes it has sufficient information to complete the HBCD risk evaluation using a weight of the scientific evidence approach in light of the limited time available under the statute for completing the risk evaluation. EPA selected the first 10 chemicals for risk evaluation based in part on its assessment that these chemicals could be assessed without the need for regulatory

	quotients, that HBCD presents unreasonable environmental risks.	information collection or development. When preparing this risk evaluation, EPA obtained and considered reasonably available information, defined as information that EPA possesses, or can reasonably obtain and synthesize for use in risk evaluations, considering the deadlines for completing the evaluation. EPA has improved the discussion of modeling uncertainties throughout the risk evaluation. EPA provides model assumptions used to predict surface water, sediment and soil concentrations in Section 2.3. In response to these comments, EPA has revised and clarified the language used in the unreasonable risk determinations in Section 5. The environmental risk determination in the final draft risk evaluation has been updated to utilize the more robust and sensitive 10^{th} percentile flow rate value for environmental exposure.

Human Health Risk Characterization - Public and Peer Review Comments		
Charge Question 10.1: Please comment on EPA's approach. **Charge Question 10.2:** Please comment on EPA's approach.		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 10**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 10.1		
SACC	**SACC COMMENTS:** • The EPA should calculate MOEs both with and without the use of appropriate PPE. This includes the use of personal protection face masks (*i.e.*, respiratory protection) for inhalation exposures and the wearing of gloves for dermal exposures. (p. 148) • Inasmuch as regulations for the use of appropriate personal protective equipment (PPE) are in place for occupational exposures, the Committee agreed that it is appropriate for the EPA to calculate MOEs based on the diminished exposure anticipated from use of the PPE. However, some members on the Committee also noted that some workers may not use PPE at all times, even when instructed or required to do so. Accordingly, calculation of MOEs without use of PPE should be done for all routes of exposure. The EPA did this for the use of respiratory protection with regard to inhalation exposures but chose not to do this for the use of gloves with regard to dermal exposures. (p. 147)	MOEs are indeed shown without expected PPE use for both inhalation and dermal exposure. Adjusted MOEs are also shown for expected respirator use, while the risk evaluation states that impervious gloves are expected to fully eliminate dermal exposure. Risks have already been calculated without PPE. There are no MOEs to calculate with the use of impervious gloves, because exposure is expected to be negligible.
SACC	**SACC COMMENTS:** • In considering different lifestages, the EPA should follow the DHHS guidelines and consider adults as those age 18 years and higher. (p. 148) • The Committee noted both a lack of consistency throughout the document and with the Department of Health and Human Services (DHHS) standard of age 18 years as the division between children and adults: The document uses age 16 years in some places and ages 18 or 21	The terminology for adults vs children has been corrected throughout the document when necessary.

	years in other places. (p. 147)	
SACC	**SACC COMMENTS:** • The EPA should clearly cross-reference information provided in supplemental documents in the main document when they provide explanation, justification or other experimental support for a key choice of hazard endpoint or critical study. (p. 148) • Much of the supporting, mechanistic information from the published literature is not included in the main document but is provided in multiple supplemental documents. It was noted, however, that no or little direct reference is made to this supporting information in the main document (pp. 147-148)	A distinct mechanistic information section has been added for each health domain. Some information has been pulled from the supplemental document, and a reference to the supplemental document is included.
SACC	**SACC COMMENTS:** • The EPA should ensure that exposure estimates incorporate the differences in Permissible Exposure Limits (PELs) for HBCD and for PNOC in the occupational scenarios. Thus, reference to EU PEL for PNOC should be added. (p. 148) • A Committee member also noted that the EPA used industrial exposures for HBCD and particulate matter (PM) from the European Union (EU). Because there is a lower limit for occupational exposures to PNOR in the EU (*i.e.*, 10 mg/m^3 8-hour TWA) than OSHA's PEL (*i.e.*, 15 mg/m^3 8-hour TWA), exposures are controlled to a lower level in the EU, so that use of these data might underestimate U.S. worker exposure. This issue is further discussed in the response to Question 5. (p. 148)	EPA revised Section 2.4.1.14, Assumptions and Key Sources of Uncertainties for Occupational Exposures, and discussed European occupational exposure limits in this section. Specifically, EPA stated that the extent to which the monitoring data pertaining to workers in Europe represent the distributions of inhalation exposure air concentrations pertaining to workers in the U.S. is uncertain. Furthermore, the reason for this uncertainty is that the determinants of HBCD occupational exposure in Europe and in the U.S. may not be similar. These determinants include the engineering controls which in Europe and in the U.S. may be different due to differing occupational exposure limits.
SACC	**SACC COMMENTS:** • The EPA should perform additional sensitivity analysis based on differences in mobility in subpopulations with varying socioeconomic status. (p. 148)	Longer residency times would not increase exposure, as the longer residency results in reduced integrated exposure since exposure decreases with aging through lifestages. As explained above, lower mobility will decrease

	• In describing lifestage susceptibilities and chronic exposures to HBCD, the EPA made assumptions based on population mobility. A Committee member noted a concern that individuals from lower socioeconomic groups will likely have lower mobility, thus prolonging their exposure to HBCD. (p. 148)	exposure. The 13-year weighted average exposure estimate represents a worst-case scenario, integrating exposure from birth through age 13. Any subsequent years of adult exposure would reduce the weighted average dose because dose is per kg body weight. These preexisting conditions have been added to the PESS discussion in Section 3.2.7.
SACC	**SACC COMMENTS:** • The EPA should more carefully evaluate the levels of risk for installation and demolition conditions of use. (p. 149) • Each of these exposure scenarios are clearly described and the nature of potential exposures are mostly clearly justified. A concern was noted, however, about the decision of no unreasonable risk for installation and demolition conditions of use. (p. 147)	Releases and downstream general population exposures/risk estimates have been recalculated for these COUs. For workers within these COUs, based on SACC comments EPA has determined that regular respirator use is unlikely and unreasonable risk was identified for these COU in the Final Risk Evaluation.
SACC	**SACC COMMENTS:** The EPA should add consideration of the impact of specific preexisting conditions that result in increases in liver fat content, as these could impact HBCD retention and thus change biologically effective exposure and the risk. (p. 149) • Besides socioeconomic status, a Committee member also noted the absence of consideration of specific preexisting conditions, such as obesity, metabolic disease, hypercholesterolemia, non-alcoholic fatty liver disease, alcoholic liver disease, and Hepatitis C and B viral infections that may result in increases in liver fat content. Such conditions could impact HBCD retention and thus increase effective exposure and risk. (p. 148)	Considerations for increased liver fat content have been added to both PESS and WOE sections.
SACC	**SACC COMMENTS:** • The EPA should give special consideration to specific populations (*e.g.*, tribal, arctic inhabitants, etc.) who depend on fish as a major source of food because of cultural considerations and provide some quantitative	A new table containing risk estimation for subsistence fishers based on three different potential HBCD concentrations in edible fish has been added to fill this gap.

	sense of how much extra risk exists for these populations. (p. 149) • It was also noted that while fish consumption as a source of exposure to HBCD is explained and described, the document does not consider certain populations whose consumption of fish is especially high due to cultural practices (*e.g.,* Native American subsistence fishers). (p. 148)	
SACC	**SACC COMMENTS:** • The EPA should consider immunotoxicity as an additional health endpoint of HBCD exposure. (p. 149) • The Committee generally agreed that the use of health effects, including developmental, thyroid, liver and reproduction seems appropriate, with perhaps additional consideration of immunotoxicity as an endpoint. (p. 147)	EPA has confirmed its original determination that the data is too limited and variable to consider immunotoxicity as a formal adverse outcome. As discussed in Section 3.2.4.1.6, the data are inconsistent in terms of cytokine stimulation, organ weights, hematology, or histopathology, with limited data on functional immune outcomes for early-life exposure.
SACC	**SACC COMMENTS:** • The EPA should consider adding a discussion of known effects of PCBs on brain signaling, Ca and Zn status, and oxidative stress, as they may have relevance to HBCD. (p. 149) • Finally, although it is recognized that little knowledge is available about the MOA for HBCD, it was noted that HBCD is structurally/chemically similar to PCBs. Recently reported effects of PCBs on brain signaling and calcium (Ca), zinc (Zn) ions, and oxidative stress as these effects for PCBs could have relevance to HBCD. Such effects could contribute to neurodevelopmental effects. (p. 148)	Data from PCBs and other thyroid disruptors are cited as evidence that HBCD can have acute effects on thyroid function and hormone levels.
SACC	**SACC COMMENTS:** • Provide further evaluation and justification for thyroid endpoint. o Concerns were expressed by some members of the Committee, however, regarding the use of thyroid effects as the most sensitive hazard endpoint following acute HBCD exposures. These	See responses in the human health hazard section. EPA has added additional detail throughout the thyroid WOE section and human health hazard uncertainties section. Additionally, EPA has clarified that the thyroid hormone changes are of most concern

	concerns relate to the lack of clear effects on thyroid hormone status or function in exposed humans and the high degree of uncertainty with this endpoint due to potential physiological differences between humans and rodents with respect to regulation of thyroid function. (p. 147)	for developmental effects, and existing evidence does not suggest that rodents are more sensitive than humans for developmental thyroid hormone changes.
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 10**	**EPA/OPPT Response**
General		

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	PUBLIC COMMENTS:
	• EPA underestimates human exposures to HBCD and fails to consider risks to potentially highly exposed and susceptible subpopulations.
	• EPA lacks necessary information concerning HBCD's carcinogenicity and other effects to sufficiently evaluate human health risks.
	• The estimated MOEs are below the benchmark MOE for young toddlers under 4 of 12 evaluated sub-scenarios and EPA failed to list these estimates.
	  ○ The MOE exceedances in infants are of particular concern to tribal populations.
	  ○ If the factor between the point of departure and the exposure (the MOE which EPA is using for their risk assessment) was made to be 1000 based on increased susceptibility due to exposure during early life stages, there would be more risks of concern identified.
	  • This is also true for acute inhalation exposures and chronic exposures related to fish ingestion for consumers.
	• Out of all of the populations EPA identifies with greater susceptibility, only one (female workers of reproductive age) is addressed in the quantitative calculation of risk.
	  ○ Further rationale for only evaluating one susceptible subpopulation quantitatively should be provided.
	• It is reported that "Risk estimates for female workers of reproductive age were 10% lower than workers overall…"
	  ○ It is unclear how EPA derived this 10% difference; data supporting the assumption that pregnant women would only be 10% more susceptible to HBCD than other workers should be provided.
		EPA evaluates PESS groups including workers, the general population living near a point source of HBCD, and consumers. EPA considers multiple susceptible populations in its development of risk estimates including women of childbearing age, all lifestages, obese individuals, individuals with pre-existing health conditions, and genetic predispositions. Subsistence fishers have been added to the final risk evaluation as an additional PESS, who have increased fish ingestion similar to tribal populations as described in Section 4.4.1.
		
		Based on mixed genotoxic data across both mammalian and non-mammalian systems and a single carcinogenicity study report, EPA does not expect that any single additional study would result in adequate evidence for carcinogenicity of HBCD.
		
		This final Risk Evaluation covered numerous exposure sub-scenarios, health effects, PESS groups, and lifestages. Risk was quantitatively assessed for various PESS groups, which includes workers. EPA attempted to be concise where possible by providing both a mid-range and high-end subscenario risk estimate for the general population, consistent with the occupational evaluation which provides a central tendency and high-end value. EPA did indicate how many of the subscenarios demonstrate risk. Of note, risk was

29,55 59	• TSCA requires EPA to protect workers. TSCA risk evaluations must also analyze risks to "potentially exposed or susceptible subpopulation[s]" who, "due to either greater susceptibility or greater exposure, may be at greater risk than the general population of adverse health effects from exposure to a chemical substance." The statute specifically defines "potentially exposed or susceptible subpopulation" to include "workers." • In the absence of quantitative data on HBCD toxicity in these populations, EPA should use established health-protective default factors in the calculation of risk to account for increased susceptibility, as recommended by the National Academies of Sciences (NAS).	identified only for a minority of the subscenarios for only a single occupational exposure scenario, and only following acute exposure. In the draft risk evaluation EPA stated that there is significant uncertainty associated with acute exposures via fish ingestion likely to overestimate risks, and this has been further clarified in the final risk evaluation. Differences in risk estimates for female workers are based on increased relative dose based on reduced body weight compared to men. As stated above, EPA considers multiple PESS groups in its development of risk estimates including women of childbearing age, all lifestages, obese individuals, individuals with pre-existing health conditions, and genetic predispositions. EPA does not necessarily provide distinct risk estimates for each subpopulation, because some are already represented by the risk estimates presented (*e.g.*, evidence suggests that liver toxicity is likely only of real concern for those with a high-fat diet or previous liver condition) while others are not quantifiable (*e.g.*, genetic predisposition, other health conditions). Subsistence fishers have been added to the final risk evaluation as an additional susceptible population. EPA does use a default intraspecies uncertainty factor of 10 to account for human variability.
MOA		
59 59	**PUBLIC COMMENTS:** • EPA should not use an MOE approach, and instead should use a unified linear approach for dose-response analysis and risk calculations for all carcinogens and non-carcinogens. • It is recommended that a unified approach to analyzing health effects from chemical exposures that applies the methods used for mutagenic carcinogens to non-mutagenic carcinogens and non-cancer health effects be applied. ○ Science indicates that a linear presumption with no threshold is	EPA relied on existing accepted guidance (*e.g.*, (EPA, 2012a, 2005a, 2002)) to evaluate noncancer and cancer endpoints in the current risk evaluation of HBCD. These methods include PBPK models for chronic endpoints that use HBCD-specific distributional information on toxicokinetics among rodents and humans; appropriate uncertainty factors for non-cancer endpoints; and a linear low-dose extrapolation to model risk from cancer, based on a

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	appropriate regardless of a carcinogen's MOA.
	• The default approach to the dose response for all MOAs should be linear.
	  ○ Assigning "nonlinear" MOAs does not account for mechanistic factors that can create linearity at a low dose, such as when an exposure contributes to an existing disease process.
	  ○ Human variability with respect to the individual thresholds for a nongenotoxic cancer mechanism can result in linear dose-response relationships in the population.
	  ○ In animal tests, a specific chemical may cause cancer through a nonlinear dose-response process. But for the human population, the dose-response relationship for the same chemical is likely a low-dose linear one, given the high prevalence of pre-existing disease and background processes that can interact with a chemical exposure, and given the multitude of chemical exposures and high variability in human susceptibility.
	• Chemical exposures that add to existing (background) processes, endogenous and exogenous exposures lack a threshold if a baseline level of dysfunction occurs without the toxicant and the toxicant adds to or augments the background process.
		likely genotoxic MOA. EPA believes that these methods adequately account for variability and susceptibility within the population, a concern raised by NRC (2009). However, EPA will investigate additional scientific approaches for EPA's next set of TSCA risk evaluations.

MOE		

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	<u>PUBLIC COMMENTS:</u>
	• Margins of Exposure (MOEs) do not provide a risk estimate but are a single number similar to a Reference Dose; this restrictive approach does not provide information about the magnitude of the risks above, at, or below a certain level.
	  ○ It implies that there is a "safe" level of exposure below which no harm will occur, which is an invalid assumption.
	
	• Although EPA considered fish consumption of tribal populations, in the estimates of HBCD exposure via fish ingestion, tribal chronic exposure is not evaluated.
	  ○ EPA stated that the upper end estimate for residential mobility is 33 years and selected that value for a high-end exposure duration. Tribal people are highly exposed for their lifetime and thus much longer than this 33-year estimate.
	  ○ EPA uses a central tendency estimate for residential mobility of
		Under TSCA, EPA is evaluating unreasonable risk. The magnitude of risks is considered in the determination of unreasonable risk and will influence the risk management options undertaken for any COU found to exhibit unreasonable risk. EPA does not state that MOEs above a benchmark imply an absence of potential harm. Risk is a probabilistic determination based on various assumptions.
		
		There is insufficient reasonably available data to robustly estimate tribal exposure. However, EPA is adding risk estimates for subsistence fishers to the final risk evaluation based on a range of HBCD fish tissue concentrations covering both "near-field" and "far-field" environmental exposures. The risk estimates for subsistence fishers may be applicable to

	13 years (page 233). In choosing to use central-tendency fish ingestion rates for chronic exposure, EPA fails to understand the meaning of subsistence users and tribal lifeways. Tribal people who live on their tribal lands tend to live there throughout their lives, which are typically much longer than 13 or even 33 years. ▪ Chronic exposure evaluations for tribal populations using high-end fish ingestion rates and lifetime exposure assumptions must be included in the final risk evaluation.	certain tribal populations.
24, 57	**PUBLIC COMMENTS:** • In EPA's evaluation, MOEs are well below benchmark levels for most inhalation workplace scenarios and health effects; for dermal contact, the MOEs often approach or are below 1, meaning that there is little or no difference between anticipated worker exposure levels and concentrations known to cause adverse effects. o In order to conclude that MOEs will be reliably above the risk benchmarks, EPA assumes use of PPE, both respirators and gloves. o MOEs for respiratory scenarios are only valid under the assumptions that: ▪ Workers are properly trained and fitted on respirator use, and that they wear respirators for the entire duration of the work activity. ▪ Workers and occupational non-users wear respirators for the entire duration of the work activity throughout their career. ▪ Similar assumptions apply to the use of gloves and their expected elimination of any dermal exposure. ▪ These are unlikely scenarios and therefore the determination of no unreasonable risk is not supported. • EPA should clearly state that its risk F for those conditions of use is predicated upon the use of the PPE to mitigate the risks identified. • EPA must base its risk determinations for workers on the assumption that PPE is not protective and	EPA generally assumes compliance with OSHA requirements for protection of workers, including the implementation of the hierarchy of controls. In support of this assumption, EPA used reasonably available information, including public comments, indicating that some employers, particularly in the industrial setting, are providing appropriate engineering or administrative controls or PPE to their employees consistent with OSHA requirements. EPA does not have reasonably available information to support this assumption for each COU; however, EPA does not believe that the Agency must presume, in the absence of such information, a lack of compliance with existing regulatory programs and practices. Rather, EPA assumes there is compliance with worker protection standards unless case-specific facts indicate otherwise, and therefore existing OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE in a manner that achieves the stated APF or PF. EPA's decisions for unreasonable risk to workers are based on high-end exposure estimates, in order to account for the uncertainties related to whether or not workers are using PPE. EPA believes this is a reasonable and appropriate approach that accounts for reasonably available information and professional judgment related to worker protection practices, and addresses uncertainties regarding availability and use of PPE.

	examine the magnitude of exposure and risk in the absence of PPE. ○ EPA should provide evidence that workers are adequately using PPE. EPA should visit user facilities to determine whether and when PPE is in use.	
31 31	**PUBLIC COMMENTS:** • In the "import" condition of use, (Import: RQ = 5.03 // MOE = 1/300 (no PPE)), EPA highlights the MOE for no PPE rather than for when PPE is in fact used, and should clarify whether the "no unreasonable risk" finding is based on no PPE usage. ○ The agency provides only a brief explanation in the "risk considerations" section and does not tie the finding of no unreasonable risk to any particular factor. EPA should provide a clear description of the factors that drive the risk conclusions.	Unreasonable risk findings are based on reasonable expectations of PPE usage. EPA assumes reasonable PPE usage includes respirators up to APF=50 and glove use for all COU except installation and demolition of XPS/EPS insulation. For solid particulates such as HBCD, proper glove use is expected to fully mitigate dermal exposure. EPA has outlined its PPE assumptions in Section 5.1 and has supplemented some sources and information on respirator use in Section 2.4.1.1. of the Risk Evaluation. EPA has also added a table in Section 4.2.2 to make the PPE assumptions made for each COU clearer. For the purposes of determining whether a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are described in the unreasonable risk determination for each condition of use, in Section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
Modeling		
28, 33, 48	**PUBLIC COMMENTS:** • The lack of sufficient cancer bioassay data warrants an additional UF of threefold for data deficiencies when determining the Benchmark MOE	There is no universal list of hazard data required when evaluating chemical risks under TSCA. Furthermore, for HBCD, EPA had sufficient, reasonably available

	for both acute and chronic exposure durations, and for all routes, and for all of the (sub)populations included in the risk evaluation. ▪ Thus, the Benchmark MOEs for all exposure scenarios (endpoints, routes and populations) should be increased at least threefold, although one could argue for a tenfold UF as well. ▪ Application of an additional 3-fold UF would result in the following changes to the determinations of unreasonable risk: o Fourteen (14) scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Acute Inhalation Exposures, Occupational Scenarios (Table 4-9). o Twenty-five (25) scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Chronic Inhalation Exposures, Occupational Scenarios (Table 4-10). o No (0) scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Acute Dermal Exposures (Table 4-11). o Eleven (11) scenarios shift to Unreasonable Risk in the Risk Estimation for Workers Non-Cancer Effects Following Chronic Dermal Exposures in Occupational Scenarios (Table 4-12). o No (0) scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects – General Population (Table 4-13). o Four (4) scenarios shift to Unreasonable Risk in the Risk Estimation for Non-Cancer Effects Following Acute Exposure to Highly Exposed Population (Table 4-14). o No (0) scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Acute Exposure to Highly Exposed Population – Inhalation (Table 4-15). o No (0) scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Acute Exposure to Highly Exposed Populations Consumer Articles (Table 4-16). o Seven (7) scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Chronic Exposure to Highly Exposed Population (Table 4-17). o No (0) scenarios shift to Unreasonable Risk in the Risk Estimate for Non-Cancer Effects Following Chronic Exposure	hazard information to conduct a risk evaluation and support the use of the chosen hazard endpoints. Therefore, EPA did not use a database uncertainty factor in the HBCD risk evaluation. EPA may consider various options for visual

31, 51	to Highly Exposed Populations Consumer Articles (Table 4-18). • EPA should consider using other risk assessment models such as HESI's Risk21 Project and Web Tool to help communicate results of the risk evaluation. This web tool provides a clear and effective visual representation of the range of potential risks that is particularly effective for risk communication purposes.	presentation and communication of hazard and risk data in the future.
24, 57 24, 57 24, 57	**PUBLIC COMMENTS:** • EPA acknowledges that it is "unable to model the potential effects of bioaccumulation in human tissues over time" and elsewhere recognizes that levels of accumulation are highly variable within the human population. o The Uncertainty Factors (UFs) currently applied to compensate for these uncertainties are not sufficient. o The conclusion that the buildup in body burden from long-term general population and consumer exposure scenarios will not present an unreasonable risk is flawed and should be reexamined. • The UFs EPA uses to calculate benchmark MOEs do not reflect EPA's recognition it lacks sufficient data to reach a determination concerning HBCD's immunotoxicity, male reproductive effects, and carcinogenicity, and that it cannot address developmental neurotoxicity risks because of "inconsistencies and/or limitations with the database." o These are serious database deficiencies that, under EPA guidance, should result in an additional UF of 10X. • EPA relies on the standard 10X Uncertainty Factor (UF) for extrapolating from subchronic studies to chronic exposure. o However, EPA is applying this standard UF already because it is using a non-lifetime study to predict adverse effects of a chemical over a lifetime.	The addition of extra uncertainty factors for bioaccumulation is not addressed in any EPA guidance documents. While EPA acknowledges that there is significant uncertainty associated with the bioaccumulation potential of HBCD, use of an additional 10x without any data supporting that value would not reduce uncertainty. EPA attempted to account for the inability to model the impact of bioaccumulation in human tissues by "utilizing the upper range of absorption estimates across available studies and including a 10x subchronic to chronic UF." EPA also conservatively evaluated risks to all receptors from hazards only observed in the F2 population (*i.e.,* only after 2 generations of bioaccumulation). Additionally, EPA conservatively considered acute risks for developmental effects not typically associated with acute exposure based on the persistence of HBCD within tissues. There is no universal list of hazard data required when evaluating chemical risks under TSCA. Furthermore, for HBCD EPA has sufficient, reasonably available hazard information to conduct a risk evaluation and support the use of the chosen hazard endpoints. Therefore, EPA did not use a database uncertainty factor in the HBCD risk evaluation.

General Risk Characterization – Public Comments		
Charge Question 11.1: Please comment on the objectivity of the underlying data used to support the risk determinations and the sensitivity of the agency's conclusions to analytic assumptions made. **Charge Question 11.2:** Please comment on the characterization of uncertainties and assumptions including whether EPA has presented a clear explanation of underlying assumptions, accurate contextualization of uncertainties and, as appropriate, the probabilities associated with both optimistic and pessimistic projections, including best-case and worst-case scenarios. **Charge Question 11.3:** Please provide information on additional uncertainties and assumptions that EPA has not adequately presented. **Charge Question 11.4:** Please comment on whether the information presented supports the findings outlined in the draft risk characterization section. If not, please suggest alternative approaches or information that could be used to develop a risk finding in the context of the requirements of the EPA's Final Rule, Procedures for Chemical Risk Evaluation Under the Amended Toxic Substances Control Act (82 FR 33726).		
#	**Summary of Peer Review Comments for Specific Issues Related to Charge Question 11**	**EPA/OPPT Response**
Summary of Peer Review Comments for Specific Issues Related to Charge Question 11.1		
General		
SACC	**SACC COMMENTS:** • The Committee suggested that for future reviews that EPA make available their summarizing PowerPoint presentations prior to the meeting. Committee members would greatly benefit from having access to the summary slide presentation to help guide them through the corresponding Evaluation and supplemental files. This will be especially helpful given the very tight timeline anticipated for completing reviews. (p. 150)	In future peer review meetings, EPA will strive to provide more timely presentation materials to the SACC.
Reconsider PPE assumptions		
SACC	**SACC COMMENTS:** • Reconsider assumptions of appropriate PPE use. ○ A shared concern of many Committee members was that there are no data to support the key assumption that potentially exposed workers would necessarily wear protective equipment and use PPE. Assumptions of appropriate PPE use in the primary manufacturing workplace, and more significantly, in post-manufacturing situations (demolition, disposal, recycling) are	EPA generally assumes compliance with OSHA requirements for protection of workers, including the implementation of the hierarchy of controls. In support of this assumption, EPA used reasonably available information, including public comments, indicating that some employers, particularly in the industrial setting, are providing appropriate engineering or administrative controls or PPE to their employees consistent with OSHA requirements. EPA

	unrealistic and would lead to an overall underestimation of exposure for human receptors. This was viewed as a weakness of the risk evaluation that contributed significant uncertainty to the overall risk characterization. (p. 152) • Second alternative from above: Lacking data to demonstrate that workers actually use PPE to the extent assumed in the Evaluation, a more acceptable alternative is to determine what is reasonable use of PPE and base the assessment on that assumption. • Referencing material safety data sheet (MSDS) information as the criteria or simply stating current "best practices" is insufficiently precise and represents an unrealistic approach to risk assessment. (p. 156) • Another approach suggested would be to ask the authors of the referenced monitoring studies about observed use of PPE during their project. Given this observational information is very subjective and subject to error, many concluded that this information would not be acceptable as "data" for a science-based risk assessment. (p. 156) • Published literature and NIOSH might provide some generic data on use of PPE in certain industries such as construction (see discussion in Q1.1). (p. 156)	does not have reasonably available information to support this assumption for each COU; however, EPA does not believe that the Agency must presume, in the absence of such information, a lack of compliance with existing regulatory programs and practices. Rather, EPA assumes there is compliance with worker protection standards unless case-specific facts indicate otherwise, and therefore existing OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE in a manner that achieves the stated APF or PF. EPA's decisions for unreasonable risk to workers are based on high-end exposure estimates, in order to account for the uncertainties related to whether or not workers are using PPE. EPA believes this is a reasonable and appropriate approach that accounts for reasonably available information and professional judgment related to worker protection practices, and addresses uncertainties regarding availability and use of PPE. EPA has re-evaluated its assumptions of PPE use for each occupational exposure scenario for the final risk evaluation. Based on this evaluation, EPA has concluded that workers exposed to HBCD via installation or demolition activities are unlikely to wear respirators. EPA has outlined its PPE assumptions in Section 5.1 and has supplemented some sources and information on respirator use in Section 2.4.1.1. of the Risk Evaluation. EPA has also added a table in Section 4.2.2 to make the PPE assumptions made for each COU clearer. For the purposes of determining whether a condition of use presents unreasonable risks, EPA incorporates assumptions regarding PPE use based on information and judgment underlying the exposure scenarios. These assumptions are

		described in the unreasonable risk determination for each condition of use, in Section 5.2. Additionally, in consideration of the uncertainties and variabilities in PPE usage, EPA uses the high-end exposure value when making its unreasonable risk determination in order to address those uncertainties.
Consider additional data		
SACC	**SACC COMMENTS:** • Consider additional peer-reviewed literature that may be relevant. o Despite the overall improvements stated above, the Committee raised several concerns with the approach used by the EPA to screen and evaluate the relevant research literature on HBCD. In particular, the initial data search strategy was viewed by many Committee members as too restrictive and resulted in exclusion of a large body of relevant information that EPA did not consider in the initial data search. For example, there exists an extensive peer-reviewed literature on "respirator use industry"[12] that can be readily accessed through a PubMed search that would likely have served to better inform and guide EPA on the potential effects of exposure controls using reliable data rather than relying on many assumptions. (p. 150)	EPA will consider inclusion of information on engineering controls and PPE usage in the literature search strategy for future evaluations.
SACC	**SACC COMMENTS:** • Consider using high-quality data for related persistent organic pollutants to estimate HBCD half-lives. o Another weakness of the risk characterization is that the estimates of HBCD half-life in several environmental compartments, including the built environment, relies heavily on unsubstantiated assumptions. No attempt is made to draw from the rich data that exists for related persistent organic pollutants with similar physicochemical properties and use patterns (*e.g.,* polybrominated diphenylethers, polychlorinated biphenyls), whose half-lives have been accurately measured to be on the order of years, rather than weeks as suggested for HBCD. Such omissions of high-quality	Although the polybrominated diphenylethers and polychlorinated biphenyls are also persistent and bioaccumulative, EPA's PECO and screening criteria relied only on studies of acceptable quality on HBCD itself for the final Risk Evaluation. EPA used the Office of Pesticide Program *guidance Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation.* The Standard Operating Procedures were developed by scientists from USEPA and the Pest Management Regulatory Agency of Health Canada in order to standardize approaches to characterize pesticide

	data are likely to influence the HBCD Evaluation and in turn weaken several of the conclusions about general risk characterization. (p. 152)	biodegradation rates and half-lives. It employs state of the science methodologies to derive data for use in pesticides assessments by NAFTA partners These procedures allow for the determination of the appropriate kinetics and associated half-lives for biodegradation studies. The guidance allows for a 3X factor to be used to account for uncertainty and variability where only 1 half-life value is available. In the final Risk Evaluation, the 3X factor was used with the longest reported half-life from Davis (2006) to give a half-life of 384 days. EPA believes the use of the longer half-life addresses concerns that an insufficiently conservative half-life was used. EPA conducted a sensitivity analysis using the range of reported half- lives including 384 days to determine the impact of half- life on modeled sediment concentrations. The results are presented in Section 2.13 Assumptions and Key Sources of Uncertainty for Fate and Transport Table 2-4 and further discussed in Section 4.1 Environmental Risk.
Clarifications		
SACC	**SACC COMMENTS:** • Clarify objectivity of criteria used for data/information collection o The Committee expressed grave concerns that subjective rather than empirical criteria were used during the data and information collection phase (Section 1.5). It was unclear whether a set of objective inclusion/exclusion criteria were set out prior to selecting 71 of 1,796 references to assess environmental fate and transport (Figure 1-6), 26 of 1847 references to assess environmental releases and occupational exposure (Figure 1-7), 345 of 1,208 references to assess general population, consumer and environmental exposures (Figure 1-8), 48 of 630 sources to assess environmental hazard (Figure 1-9), and 51 of 1890 studies to assess human health hazard (Figure 1-10). (p. 151)	The criteria utilized for screening of literature search results for relevance was published in *The Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a) document. Screening criteria were used to establish relevance of identified studies and are independent from the data evaluation step. EPA's systematic review process is currently being reviewed by NAS and improvements will be made in the future based on this feedback.
SACC	**SACC COMMENTS:**	These sources were used for identifying highly

	• Clarify how data from existing assessments was used in HBCD risk assessment. ○ The Committee was encouraged that EPA considered key and supporting studies from existing assessments (*e.g.*, EPA IRIS assessments, ATSDR assessments, ECHA dossier), however, there is a lack of clarity about when and to what extent data contained within these key reports were included or excluded in the HBCD assessment. (p. 151)	relevant "key and supporting" literature that was likely to be important for dose-response analysis or weight-of-evidence. These studies were evaluated through the TSCA data quality evaluation criteria, independently of their original evaluation or utility in the previous assessments. Additional supporting information not included in the primary Risk Evaluation document has also been included in the Human Health Hazard supplemental document.
SACC	**SACC COMMENTS:** • Clarify objectivity of criteria used for data/information collection. ○ The Committee expressed grave concerns that subjective rather than empirical criteria were used during the data and information collection phase (Section 1.5). It was unclear whether a set of objective inclusion/exclusion criteria were set out prior to selecting 71 of 1,796 references to assess environmental fate and transport (Figure 1-6), 26 of 1847 references to assess environmental releases and occupational exposure (Figure 1-7), 345 of 1,208 references to assess general population, consumer and environmental exposures (Figure 1-8), 48 of 630 sources to assess environmental hazard (Figure 1-9), and 51 of 1890 studies to assess human health hazard (Figure 1-10). (p. 151)	The criteria utilized for screening of literature search results for relevance was published in *The Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a) document. EPA's systematic review process is currently being reviewed by NAS and improvements will be made in the future based on this feedback.
SACC	**SACC COMMENTS:** • Clarify how scoring system was used in HBCD systematic review. ○ Although discussed at several points during the Committee's deliberation, it remained unclear the extent to which the scoring system used to include or exclude data and data sources impacted the initial evaluation and risk characterization. This lack of clarity increased the Committee's concern that relevant studies of high-quality may have been excluded. The Committee was not confident that the review faithfully followed the protocols and metrics described in the TSCA systematic review document. The Committee and public commenters questioned the objectivity of the TSCA systematic review protocol, considering it still too	The criteria utilized for screening of literature search results for relevance was published in *The Application of Systematic Review in TSCA Risk Evaluations* (U.S. EPA, 2018a) document. EPA's systematic review process is currently being reviewed by NAS and improvements will be made in the future based on this feedback. Data quality evaluations for all individual relevant studies are provided in the Supplemental documents, containing a breakdown of every scoring metric. Studies were only excluded as "not relevant" based on a screening of the title and abstract for relevance

	subjective, not based on clearly defined study quality parameters, and in general not empirical. Some Committee members felt that the approach used in the Evaluation increases uncertainty across several components of the overall risk characterization for HBCD, and likely contributes to underestimates of risk.	to HBCD risk evaluation, not based on data quality.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 11.2		
General		
SACC	**SACC COMMENTS:** • Consider including approaches to quantify uncertainties. o Throughout the draft Evaluation, characterization of uncertainties is qualitative and only minor efforts are made to demonstrate uncertainties quantitatively. In many incidences EPA might not have sufficient data to conduct quantitative (probabilistic) assessment of uncertainties; but in some cases EPA appeared to have a range of values (*e.g.*, estimated environmental release, half-life time, dermal absorption rate, etc. see for example Table_Apx F-3 and Table_Apx F-4) that allow for quantitative assessment of the impact of the assumptions or choice (*e.g.*, mean vs 90th percentile) on associated estimation, and also assessment of how the uncertainties might propagate downstream to further affect the final risk value. Taking mouthing as an example of exposure route, EPA has a reasonable estimate of the distribution of exposure and could have conducted a sensitivity analysis by using multiple values along this distribution as an estimated exposure level. Table 4-13 displays only central tendency estimates, but no high-end estimate. The Committee encouraged EPA to develop a practical and sensible process whereby uncertainties are quantified systematically and consistently. The present Evaluation of HBCD presents such an opportunity to do so. (pp. 153-154)	Table 4-13 only presented high-end estimates previously. Central tendency dermal exposure and risk estimates have since been added to the final risk evaluation (now Tables 4-16 and 4-17). EPA evaluated risks to workers based on a quantitative range of estimates for most OES (*i.e.*, High-End and Central-Tendency). While environmental/general population exposures were not probabilistically analyzed, EPA did assess risks based on various sub-scenarios that capture variability in the most sensitive parameters. For PESS exposure scenarios such as children's mouthing (and infant aggregate exposure), EPA provided risk estimates for the worst-case exposure scenario in order to evaluate the most protective situation. In these cases, risks were not identified even using worst-case assumptions, so providing risk estimates for lower-level exposures was not necessary.
Reconsiderations of data currently used		
SACC	**SACC COMMENTS:** • There was extensive discussion among Committee members in Question	Delayed eye opening has been added as an endpoint and POD to the risk evaluation. However, 1500 ppm

	8 (Human Health Hazard - Section 3.2 of the Draft Risk Evaluation) as to the appropriateness and validity of using 15,000 ppm (high dose exposure group) as the point of departure (POD) for the thyroid hormone (TH) effects from Ema et al., (2008). Committee members strongly recommended that EPA reconsider using the 1500 ppm dose (*e.g.*, delay in eye opening) as the POD for risk characterization. Perhaps both analyses should be included by amending the appropriate tables and text in the main report. At the very least, a stronger, more convincing, rationale should be offered to justify use the 15,000 ppm data as a POD. (p. 152)	is not used as a POD because BMD modeling is a more precise approach that was used to derive PODs for all endpoints from Ema et al., (2008). 15,000 ppm was never used as a POD. EPA derived multiple BMDLs for thyroid hormone changes (a BMDL10 of 22.5 mg/kg was the most sensitive) and a BMDL05 of 28.73 mg/kg was used for delayed eye opening.
SACC	**SACC COMMENTS:** • Consider relevance of non-monotonic dose relationships. ○ Since several classes of chemically related persistent organic pollutants (POPs) can elicit non-monotonic ("inverted U") dose relationships in both in vivo and in vitro animal models of developmental neurotoxicity (Frank et al., 2018; Chen et al., 2017; Dach et al., 2017; Kim et al., 2011), the analysis and rationale should include Page 153 of 166 discussion of this potential response for outcomes related to changes in TH signaling (Sethi et al., 2019). (pp. 152-153)	EPA determined that this is not likely to be relevant for the particular dose-response relationships observed in this risk evaluation because none of the modeled data demonstrated a non-monotonic relationship.
SACC	**SACC COMMENTS:** • The Evaluation acknowledges that alternative adverse outcome pathways affecting neurogenesis and differentiation, calcium homeostasis, and neurotransmitter release could be contributing to HBCD adverse outcomes, however, these alternative adverse outcome pathways are afforded one short paragraph within the Evaluation (page 307), only regarding a primary TH mechanism. This underlying assumption may not be accurate, and two Committee members referred to relevant publications not considered by EPA that indicate low-dose HBCD elicits reproductive and neurodevelopmental toxicity both in vivo and in vitro mediated by alternative mechanisms. These mechanisms are elicited at much lower concentrations/doses than those reported for TH-related effects reported by Ema et al., 2008 (see Shi et al., 2019, Rasinger et al.,	Data from Rasinger et al., (2018) has been included in the Risk Evaluation. The study used only a single dose and is not usable for dose-response analysis, however data from the study has been added to the hazard ID and WOE section, where relevant. This data adds to the existing mechanistic discussion on the neurotoxicity hazard domain. For additional details on mechanistic data and MOA for each endpoint, see the supplemental file *Supplemental Information on Human Health Hazard*.

	2018; Reflatto et al., 2018, Rasinger et al., 2014). For example, similar in vivo and in vitro mechanisms of HBCD neurotoxicity have been implicated using both transcriptomic profiling in brains of female mice exposed through their diet to HBCD (199 mg/kg body weight per day) for 28 days and compared with those of neuronal N2A and NSC-19 cell lines exposed to 1 or 2 μM HBCD. Similar pathways and functions were affected both in vivo and in vitro, including Ca2+ and Zn2+signalling, glutamatergic neuron activity, apoptosis, and oxidative stress. Although most of these data were published after preparation of the EPA risk evaluation, they should be used to provide context for the limitations of the underlying assumptions and the uncertainties that arise from using the high-dose data from Ema et al., 2008 as the POD. (p. 153)	
SACC	**SACC COMMENTS:** • TH measurements and reductions produced by HBCD from the Ema et al., (2008) study should also be considered in the context of the available human epidemiology data indicating the quantitative reductions of T4 and/or increases in TSH needed to observe cognitive and behavioral impairments. This would better place the TH effects on which the developmental POD is based in the context of the human literature on hypothyroidism. (p. 153)	Section 3.2.4.1.1 and the beginning of Section 3.2.5.2.2 both address epidemiological data on thyroid hormone effects relevant to downstream neurological effects.
SACC	**SACC COMMENTS:** • Reconsider objectivity of Ema et al., 2008 study design and analysis. o There was significant discussion and concern about the objectivity of the analysis used in the developmental POD for risk characterization. Particularly concerning was the potential weaknesses of combining of F0 and F1 data from Ema et al., 2008 in order to generate a statistically significant result. The potential pitfalls of the experimental design that uses continuous dosing across F0 and F1 generations without accounting for influences of HBCD bioaccumulation across generations deserves additional discussion. (p. 153)	Based on these criticisms, the BMD modeling results that combined F0 and F1 data have been removed from consideration for dose-response analysis in the risk evaluation, and this endpoint (reduced pregnancy incidence) is no longer represented in the dose-response analysis. EPA acknowledges that HBCD's persistent and bioaccumulative properties will result in long-term exposure to HBCD, including dietary uptake via trophic transfer. EPA estimates the environmental risk to higher trophic level organisms such as American kestrel and osprey (Section 4.1.3.3) that may result from HBCD trophic transfer. However,

		the exposure factors used to quantify HBCD dietary uptake are based on monitoring data and therefore cannot be attributed to any specific release type or source.
SACC SACC	**SACC COMMENTS:** • Reconsider estimated HBCD half-lives. o The estimates of HBCD half-life in various environmental scenarios (weeks to months) reported in the Evaluation are considered unrealistic and are likely large underestimates. This is due to chemical stability issues, but also more importantly to releases into the environment from degradation of XPS and EPS into microparticles (nanoparticles) that will likely persist for many decades. (p. 154) The Committee concluded that the values presented represents a gross underestimation of the true half-life, which is likely to be measured in years if not decades. This degree of underestimation is likely to influence several aspects of risk characterization and lead to underestimation of related uncertainty. (p. 155)	In response to the SACC comment EPA further addressed uncertainty associated with biodegradation half-lives reported for HBCD by using Office of Pesticide Program guidance *Standard Operating Procedure for Using the NAFTA Guidance to Calculate Representative Half-life Values and Characterizing Pesticide Degradation*. The Standard Operating Procedures were developed by scientists from USEPA and the Pest Management Regulatory Agency of Health Canada in order to standardize approaches to characterize pesticide biodegradation rates and half-lives. It employs state of the science methodologies to derive data for use in pesticides assessments by NAFTA partners These procedures allow for the determination of the appropriate kinetics and associated half-lives for biodegradation studies. The guidance allows for a 3X factor to be used to account for uncertainty and variability where only 1 half-life value is available. In the final Risk Evaluation, the 3X factor was used with the longest reported half-life from Davis (2006) to give a half-life of 384 days. EPA believes the use of the longer half-life addresses concerns that an insufficiently conservative half-life was used. EPA conducted a sensitivity analysis using the range of reported half-lives including 384 days to determine the impact of half- life on modeled sediment concentrations. The results are presented in Section 2.13 Assumptions and Key Sources of Uncertainty for Fate and Transport Table 2-4 and further discussed in Section 4.1 Environmental Risk.
Summary of Peer Review Comments for Specific Issues Related to Charge Question 11.4		

Clarifications and enhancements		
SACC	**SACC COMMENTS:** • One Committee member suggested that the risk assessment document needs a table and associated text at the end of Section 4 to inform the reader of which scenarios discussed are associated (linked) to which combinations of life stage by category and sub-category of condition of use identified in Table 5-1. It was mentioned during the meeting that the risk determination for each combination of life stage by category and sub-category of condition of use can involve up to 32 different scenarios. As currently presented, readers are unable to determine which among the 32 scenarios drive the final risk characterization. (p. 155)	This has been included based on input and review of subsequent Risk Evaluations. Table 1-8 in Section 1.4.1 now links COUs to exposure scenarios, as does the risk conclusions summary table at the end of Section 4 (Section 4.5)
SACC	**SACC COMMENTS:** • Potential reductions in uncertainty are possible through estimation of dermal absorption via the newer more sophisticated methods measuring dermal flux parameters rather than the fraction absorbed method. (p. 155)	See Appendix L. Using high-end assumptions for estimates of flux results in the same total amount absorbed.
SACC	**SACC COMMENTS:** • Stated a few times over the course of the meeting, the Evaluation should provide additional details, clarity, or explanation on how the results of the risk characterization lead to the risk determination. In some cases, particularly for aquatic environmental risk (Section 4.1.5.2; 4.1.5.3), where multiple COU's scenarios had estimated RQ's greater than one, the process that ultimately produced a determination of "no unreasonable risk" is not clear (p. 156)	See the risk summary tables in the Risk Conclusions section, Section 4.5 for a presentation of the risk estimate values used for risk determination. This section has been added to the final Risk Evaluation.
SACC	**SACC COMMENTS:** • The description attached to the statement "does not present an unreasonable risk" should be expanded to clearly describe the uncertainty in this conclusion and the extent to which it is driven by a lack of firm data on exposures. This is especially problematical with exposures during manufacture of HBCD given the compound is no longer being manufactured in the U.S. and imports are reported as declining. (p. 92)	In response to these comments, EPA has revised and clarified the language used in the unreasonable risk determinations in Section 5.

Additional uncertainty discussion needed		
SACC	**SACC COMMENTS:** • In considering special and susceptible population exposures, more consideration needs to be given to populations with specific preexisting conditions, such as metabolic disease and obesity, as well as to tribal, ethnic and other subpopulations that depend heavily on potentially contaminated foods, such as Native American subsistence fishers. In this Evaluation, discussion is mostly confined to indicating groups potentially at greater risk, but there is no mention of how much greater these risks might be. Quantification of risk to these susceptible populations was not attempted. (p. 155)	Risks to infants and offspring are assessed through providing risk estimates for distinct lifestages in the general population assessment and to working mothers in the occupational risk assessment. An additional table of risk estimates has been included for subsistence fishers. Other PESS groups including those with preexisting conditions are discussed in Section 3.2.7.
SACC	**SACC COMMENTS:** • Overall, the Committee would have liked to have seen a more detailed discussion of mode of action (MOA) in this Evaluation. Specifically, the Committee looked for discussion of MOA for thyroid effects, but also to other mechanisms that might contribute to hepatic, reproductive and developmental toxicity endpoints. Lack of a set of acceptable MOAs should be acknowledged and factored into the uncertainty analysis (also refer to Q11.2). (p. 155)	More mechanistic data has been added, but detailed MOAs for HBCD health effects other than disruption of the HPT axis are unclear.
SACC	**SACC COMMENTS:** • Reconsider approach to developmental risks to infants. ○ A significant lack of information on toxicokinetics coupled with the fact that HBCD can cross the placenta into the fetus and be secreted in the milk to the newborn and infant both limited discussion on developmental risks to infants and raised concerns that those unassessed risks might be substantial. The final risk determination did not adequately take this into consideration but should have. (pp. 155-156)	EPA provided risk estimates for infants and all lifestages as part of the PESS group, Highly Exposed General Population. For infants specifically, EPA modeled exposures up to the 99.9%tile of aggregate exposure and did not identify risk below the benchmark MOE even at this extreme assumption. Therefore, EPA does not believe that there are any significant exposures or potential risks to infants that were not sufficiently evaluated.
PPE		
SACC	**SACC COMMENTS:** • The impact of the assumption that PPE will be used universally and appropriately has been raised by the Committee in each of the three	EPA generally assumes compliance with OSHA requirements for protection of workers, including the implementation of the hierarchy of controls. In support of this assumption, EPA used reasonably

	assessments reviewed to date. The Committee states that it is unreasonable to assume that all workers will always use PPE, but this assumption is critical to the overall conclusion that there is no unreasonable risk to the workers. This Evaluation provided RQ value for scenarios where no PPE use is assumed which allows informed comparisons with RQ values when full PPE use is assumed. This should be done consistently in TSCA evaluations. (p. 156)	available information, including public comments, indicating that some employers, particularly in the industrial setting, are providing appropriate engineering or administrative controls or PPE to their employees consistent with OSHA requirements. EPA does not have reasonably available information to support this assumption for each COU; however, EPA does not believe that the Agency must presume, in the absence of such information, a lack of compliance with existing regulatory programs and practices. Rather, EPA assumes there is compliance with worker protection standards unless case-specific facts indicate otherwise, and therefore existing OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE in a manner that achieves the stated APF or PF. EPA's decisions for unreasonable risk to workers are based on high-end exposure estimates, in order to account for the uncertainties related to whether or not workers are using PPE. EPA believes this is a reasonable and appropriate approach that accounts for reasonably available information and professional judgment related to worker protection practices, and addresses uncertainties regarding availability and use of PPE.
SACC	**SACC COMMENTS:** • The section on uncertainties should also include a statement concerning the uncertainty of regular and effective PPE regular use. (p. 156) • Revise discussions on use of PPE to clarify the impact on the risk evaluation. (p. 93)	Section 4.3.2.2 covers the uncertainty of PPE considerations. EPA determined that respirators were unlikely for demolition and construction and the risk determination now incorporates this assumption. EPA has also added a table in Section 4.2.2 to make the PPE assumptions made for each COU clearer, including exposure scenario-specific determinations of respirator use assumptions.
SACC	**SACC COMMENTS:** • The use of personal protective equipment and its impact on risk	The details of the considerations in the unreasonable risk determinations in Section 5 for each condition of use now more clearly state when EPA assumes use

	considerations needs more clarity. This is discussed in more detail in the Committee response to later questions. (p. 92)	of PPE, what APF or PF is assumed, and how the risk estimates support or do not support a determination of unreasonable risk for that condition of use. EPA also describes the other factors considered when making determinations of unreasonable risk.
Recommendations on specific sections		
SACC	**SACC COMMENTS:** • Page 376: "Based on the EPA Development Document for Effluent Limitations, Guidelines and Standards for Organic Chemicals, Plastics and Synthetic Fibers Point Source Category, 75% removal was selected as a reasonable removal estimate." The Evaluation is unclear as to whether the choice of 75% wastewater treatment (WWT) removal rate is evidence-based or simply an administrative decision. This point is important because as shown in Table Apx-K-1, MOE is proportional to WWT. Sensitivity analysis allowing this fraction to vary down to say 50% or 25% would provide information to better assess the impact of this assumption. (p. 156)	The included sensitivity analysis covered both 75% and 0% treatment removal. In the updated risk evaluation, 90% removal will replace 75%, but risk estimates will be shown for 0% as well
SACC	**SACC COMMENTS:** • Page 380: "EPA chose a BAF value at the low-end of the reported range. This was done because the modeled dissolved surface water estimates are generally larger than values reported in the literature. EPA compared the range of reported fish-tissue concentrations from monitoring data and found the modeled fish tissue concentrations (range of modeled dissolved surface water and low-end BAF) to be of a similar order of magnitude. Therefore, while selection of a different BAF value would have a significant effect on fish ingestion risk estimates, the values for BAF and resulting fish ingestion exposure are well-supported by the data." Differences in "similar order of magnitude" can be up to 10-fold, which is too big to ignore. The Evaluation should include its analysis in the report to support its choice. (pp. 156-157)	EPA selected the most robust and well-supported BAF value based on the large variability of the data. The BAF value selected has the best concordance with both the modeled results and the reported monitored exposure values from literature.
SACC	**SACC COMMENTS:** • Page 380: "ADD values representing chronic exposure utilized central-tendency fish ingestion rates, which are expected to be more	EPA acknowledges that it is possible to assess higher fish consumption. For the final Risk Evaluation EPA has added risk estimates for subsistence fishers

	representative of the most populations over a sustained period. While these assumptions are expected to protect the majority of populations, there is potential for higher risk among subpopulations with consistently elevated fish consumption rates." The Evaluation recognizes the potential for subpopulations with higher rates of fish consumption to experience higher risks, but this is not adequately discussed in uncertainty section. As mentioned in the response to a previous question, using Monte Carlo techniques, it may be possible to quantify these uncertainties in risk. (p. 157)	based on aggregate exposure assuming higher fish intake and biomonitoring concentrations instead of market food basket measurements.
SACC	**SACC COMMENTS:** • P380: "EPA believes that these sub-scenarios sufficiently capture the range of risk estimates for all reasonably expected general population exposures, with minimal remaining unaccounted-for uncertainty. Consumer article modeling defaults are believed to be highly uncertain and highly sensitive, however estimation of the risk for consumer articles were orders of magnitude above the benchmark MOE. Therefore, EPA has high confidence in the range of risk estimates for the highly exposed general population." Data and analysis are not provided to support the conclusion of "minimal remaining unaccounted-for uncertainty." The MOE for the exposed general population is being extrapolated to the highly exposed population based on its estimates for exposed general population. This needs discussion and justification. (p. 157)	The sub-scenarios cover emission factors, days of release, and wastewater treatment, which have been determined to have the greatest influence on estimates (shown in Table 2-114). Other factors only have small influence. This is all explained in that same paragraph in Section 4.3.2.5. It is incorrect that EPA simply extrapolates general population background risk to the highly exposed population. Background estimates are aggregate with COU and exposure pathway-specific exposure estimates for the highly exposed general population.
#	**Summary of Public Comments for Specific Issues Related to Charge Question 11**	**EPA/OPPT Response**
General		
31, 51 31, 51	**PUBLIC COMMENTS:** • EPA performed targeted sensitivity analyses for some, but not all, conditions of use. ○ EPA should clearly describe why was this done, how the scenarios were selected, and how the information is used to inform the overall risk characterization and risk determination. • EPA should clearly tie the conditions of use evaluated to the risk findings	Targeted sensitivity analyses were done for conditions of use in which the greatest risk was identified (i.e. exposure scenarios #1, #3, #5). For those COU in which risk was already low, providing additional risk estimates at reduced production volume and increased wastewater treatment removal would not have changed any conclusions. For those

	made for each life-cycle stage, category, and subcategory. o The Life Cycle stage categories and subcategories in Table 5-1 do not easily align with the exposure scenarios discussed earlier in the document. While Table 1-8 lists the Conditions of Use included in the Risk Evaluation, Table 4-10 is not aligned with the Risk Determination.	scenarios with high risk, it was important to determine how robust the risk conclusions were to EPA's assumptions. EPA agrees that the alignment between assessed occupational exposure scenarios (OES) and conditions of use (COU) can be improved. EPA has now clarified how the OES align to respective COUs in Table 1-8.
30, 56	**PUBLIC COMMENTS:** • TSCA requires EPA to analyze whether a chemical substance as a whole presents an unreasonable risk. o EPA must consider all conditions of use, exposures, or hazards.	Per 40 CFR 702.47 "…EPA will determine whether the chemical substance presents an unreasonable risk of injury to health or the environment under each condition of use within the scope of the risk evaluation…." This approach in the implementing regulations for TSCA risk evaluations is consistent with statutory text in TSCA Section 6(b)(4)(A), which instructs EPA to conduct risk evaluations to determine whether a chemical substance presents an unreasonable risk "under the condition of use." EPA has considered all COUs, exposures, and hazards within the scope of this risk evaluation. Additional exposure scenarios. A COU for consumer use of plastic and other articles (mouthing by toddlers) and a COU for electronics recycling have been added to the Final Risk Evaluation.
50	**PUBLIC COMMENTS:** • To mitigate risk associated with exposure to HBCD, EPA could propose a significant new use rule (SNUR) under TSCA Section 5. o The SNUR could focus on the domestic manufacture and importation of HBCD, thereby prohibiting the discontinued uses from returning without proper evaluation by the Agency.	EPA acknowledges the suggestion that EPA promulgate a Significant New Use Rule for HBCD.
Additional Clarity/Discussion Needed		
51	**PUBLIC COMMENTS:** • Under TSCA as amended, EPA does not consider risk management actions under Section 6 unless it determines that a substance presents an unreasonable risk for a condition of use (COU).	EPA has updated the unreasonable risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use.

	○ Consequently, if EPA has not established the scientific justification for the risk determinations it makes, those risk determination decisions are vulnerable to inappropriate risk management assessments. ○ EPA must substantiate all "no unreasonable risk" determinations.	
28, 33, 48	**PUBLIC COMMENTS:** • Because EPA is more likely to determine unreasonable risks for workers where risks greater than the acceptable benchmarks are identified for both central tendency and high-end exposures under the conditions of use, determination of unreasonable risk will not be made unless there are special circumstances. ○ Where the high-end scenario does not result in findings of unreasonable risk (assuming the use of PPE), EPA relies on that scenario for its risk determinations. ○ In two instances, high-end scenarios were discounted where the calculated MOE fell outside the acceptable range, and central tendency assumptions were relied on, finding no unreasonable risk. • Rationale for this approach should be provided.	EPA has updated the unreasonable risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use. EPA uses the high-end exposure value when making its unreasonable risk determination in order to address uncertainties. EPA has also outlined its PPE assumptions in Section 5.1.
31	**PUBLIC COMMENTS:** • The rationale for concluding "no unreasonable risk" where benchmarks are exceeded is not clear. ○ For example, the agency does not clarify the extent to which the lack of domestic manufacturing factors into its finding of no unreasonable risk for any particular condition of use. • The agency also does not provide alternative risk scenarios to account for potentially unknown manufacture or import by small businesses.	EPA has added additional discussion to the uncertainties section of the risk evaluation addressing the potential for unaccounted for production/ processing volume. EPA has incorporated background exposures into both the environmental and general population assessment which would account for any volume of HBCD released into the environment. EPA has updated the unreasonable risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use.

	• To address these deficiencies in its risk communication, the agency should specify a "no unreasonable risk finding driver" in the risk determination.	
50 51	**PUBLIC COMMENTS:** • EPA concluded that HBCD does not present an unreasonable risk to the general population, workers, occupational non-users, and the environment. However, additional information regarding the modeling and parameters used in the risk characterization and how this information supports EPA's risk determination conclusion is needed. o EPA should ensure that it clearly provides the scientific basis for its risk determinations in a manner that makes clear the connection between the risk characterization and the risk determination in the risk evaluation.	EPA has updated the unreasonable risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use. Additionally, EPA has added a risk conclusions section including a risk summary table that includes all risk estimates that are used for risk determination.
62	**PUBLIC COMMENTS:** • EPA lacks sufficient data to support its proposed determination of no unreasonable risk.	EPA has updated the unreasonable risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use.
62 28, 33, 48 62	**PUBLIC COMMENTS:** • EPA acknowledges that it lacks sufficient data to reach a determination concerning HBCD's immunotoxicity, male reproductive effects, and carcinogenicity. o No adequate cancer bioassays have been conducted with HBCD. ▪ Carcinogenicity data are limited to a single animal study that is "only available as an incomplete report." No epidemiological studies were identified. • Despite acknowledged data gaps, EPA still proposes a determination that HBCD presents no unreasonable risks. o Under TSCA Section 4, EPA can "require that testing be conducted on [HBCD] to develop information with respect to the health and environmental effects for which there is an insufficiency of information."	EPA did not state that it lacks sufficient data to reach a determination for weight of the evidence. EPA stated that the data supporting immune and male reproductive effects was "limited and inconsistent." Therefore the weight of the scientific evidence does not support these effects. EPA did state that there is inadequate information to assess the carcinogenic potential of HBCD, with mixed data for genotoxicity. EPA determined that the available evidence for these endpoints, in some cases limited and, in some cases, not, did not support a quantitative dose-response relationship between exposure and health outcomes. Therefore, risk estimates could not be developed for

	○ Under TSCA Section 8, EPA can require the reporting of "[a]ll existing information data concerning the environmental and health effects of [HBCD]." ○ Under Section 11, EPA can subpoena studies and other information "that the Administrator deems necessary" under TSCA. ▪ An absence of risk cannot be inferred based on an absence of information.	these outcomes and they would not be the basis of unreasonable risk
51 51	**PUBLIC COMMENTS:** • TSCA Section 26 (i) mandates that EPA make decisions under Sections 4, 5, and 6 of TSCA "based on the weight of the scientific evidence." TSCA Section 26(h) mandates that in carrying out Sections 4, 5, and 6, "to the extent that the Administrator makes a decision based on science, the Administrator shall use scientific information, technical procedures, measures, methods, protocols, methodologies, or models employed in a manner consistent with the best available science." • To meet TSCA Section 6(b)(4)(F)'s general requirements EPA must complete the following: ○ Integrate and assess available information on hazards and exposures for the conditions of use of the chemical substance (including information about specific risks of injury to health or environment and information on potentially exposed or susceptible subpopulations identified as relevant by EPA). ○ Describe whether aggregate or sentinel exposure to a chemical under the conditions of use were considered, and the basis for that consideration. ○ Not consider costs or other non-risk factors. ○ Take into account, where relevant, the likely duration, intensity, frequency, and number of exposures under the conditions of use of the chemical. ○ Describe the weight of the scientific evidence for the identified hazard and exposure.	EPA provides details on the weight of the scientific evidence for each endpoint that integrates all reasonably available information within the hazard sections (Sections 3.1.4 and 3.2.4). This data was then integrated in selecting studies and COCs/PODs for dose-response analysis (Sections 3.1.5 and 3.2.5). Aggregate and sentinel exposures are addressed throughout the document but are more specifically described in Section 4.4.2. Non-risk factors are not considered in the determination of unreasonable risk. Details about exposures to workers, the environment, the general population, and consumers are described in Section 2 including high-end and central tendency values along with various sub-scenarios for environmental exposures.
Uncertainty		

24, 57 24, 57	**PUBLIC COMMENTS:** • Compared to a typical chemical, internal doses of a bioaccumulative substance for a given administered dose will be higher over a lifetime and should further increase in later generations assuming continuing exposure. The normal and otherwise required UF of 10X to extrapolate from non-chronic studies to lifetime exposure does not account for these considerations. • EPA should thus apply an additional UF (perhaps 100X) to reflect the lifetime and multi-generational buildup of HBCD in the general population/consumers and highly exposed subpopulations due to its highly accumulative properties.	The addition of extra uncertainty factors for bioaccumulation is not recommended in any EPA guidance. While EPA acknowledges that there is significant uncertainty associated with the bioaccumulation potential of HBCD, use of an additional 10x without any data supporting that value would not reduce uncertainty. EPA attempted to account for the inability to model the impact of bioaccumulation in human tissues by "utilizing the upper range of absorption estimates across available studies and including a 10x subchronic to chronic UF." EPA also conservatively evaluated risks to all receptors from hazards only observed in the F2 population (*i.e.*, only after 2 generations of bioaccumulation). Additionally, EPA conservatively considered acute risks developmental effects not typically associated with acute exposure based on the persistence of HBCD within tissues.
PPE Assumptions		
29 29 29 29, 55	**PUBLIC COMMENTS:** • EPA should not assume consistent PPE use will eliminate the risk to workers. • TSCA requires EPA to assess worker exposure, and hence risk, without regard for the use of respirators and other PPE. • TSCA separates risk evaluation from risk management, a distinct statutory process that begins after EPA has already completed a risk evaluation and made a determination of unreasonable risk. This separation is necessary, since the selection of appropriate risk management tools requires the consideration of numerous non-risk factors including costs that cannot be considered during the risk evaluation process. • EPA determined that occupational inhalation of HBCD is responsible for risks up to 37 times greater than are acceptable, and dermal exposure results in worker risks up to 300 times above acceptable levels but determined none of these risks were unreasonable due to the assumptions that PPE will be used. • The assumption of consistent PPE use underestimates potential worker	EPA has edited the uncertainty Section (4.3.2.5) to eliminate the statement about regular use not being feasible. EPA determined that respirators were unlikely for demolition and construction and the risk determination now incorporates this assumption. EPA has also added a table in Section 4.2.2 to make the PPE assumptions made for each COU clearer, including exposure scenario-specific determinations of respirator use assumptions. These assumptions are described in the unreasonable risk determination for each condition of use, in Section 5.1. While EPA has evaluated worker risk with and without PPE, as a matter of policy, EPA does not believe it should assume that workers are unprotected by PPE where such PPE might be necessary to meet federal regulations, unless it has evidence that workers are unprotected. In consideration of these uncertainties and variabilities in PPE usage, EPA uses the high-

29	exposure and risk.	end exposure value when making its unreasonable risk determination in order to address those uncertainties.
29, 55	• The assumption that across-the-board respirator use is an adequate method of reducing chemical exposure risks is incompatible with established occupational health policy practice.	
29	• By assuming uniform use of respirators EPA avoids the obligation to establish legally binding limits on exposure to be met through more effective control measures.	Risks are presented both with and without PPE and at both high-end and central tendency exposure levels. Risk determination in the final will rely on high-end exposures for workers.
29, 55	• EPA has previously reported that respirators and other PPE were inadequate to comply with TSCA's worker protection mandate because "not all workers may be able to wear respirators" and that: o "[i]ndividuals with impaired lung function due to asthma, emphysema, or chronic obstructive pulmonary disease … may be physically unable to wear a respirator." o These workers represent a susceptible worker population. o Workers' facial hair, including beards and sideburns, can also interfere with the seal of a respirator, rendering it ineffective. o Other workers forego respirators because they "may also present communication problems, vision problems, worker fatigue, and reduced work efficiency." o Even when respirators are used, "[d]etermination of adequate fit and annual fit testing is required for tight fitting full-face piece respirators to provide the required protection."	
	• In the risk evaluation, it is recognized that "regular use of respirators in chronic scenarios may not always be feasible.	See above comment and response for further clarification on PPE assumptions.
29, 55, 59	• On the same page in the risk evaluation, it is also stated that EPA "assume[d] workers are properly trained and fitted on respirator use, and that they wear respirators for the entire duration of the work activity … throughout their career."	
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55	• EPA also speculates as to the specific types of PPE and level of protectiveness the equipment provides and assumes workers will use respirators with an APF of at least 5. o These contradictory statements must be resolved. o EPA needs to provide substantial evidence that support the assumptions that employers will provide respirators to all employees exposed to HBCD, that workers will be properly trained and fitted to use such respirators, and that workers will use such respirators throughout their work shifts.	

55 29 58	**PPE (Dermal)** • The risk evaluation states that [d]ata about the frequency of effective glove use – that is, the proper use of effective gloves – is very limited in industrial settings, and that permeable glove materials can absorb chemicals and increase worker exposures. o Improper glove use (*e.g.,* taking gloves off and putting them back on during a work shift) can also trap contaminants close to the skin and exacerbate dermal risks. • However, EPA assumes that workers will be provided and will consistently use gloves "impervious to the hazardous chemical … worn on clean hands and replaced when contaminated or compromised." o EPA assumes that gloves would eliminate any possibility of dermal exposure by nearly all workers. o These assumptions are not supported by SDSs cited in the risk evaluation. Many of the cited SDSs do not recommend specific glove materials. o EPA does not provide any support for this multi-part assumption, and it concedes that "[d]ata about the frequency of effective glove use – that is, the proper use of effective gloves – is very limited in industrial settings." o EPA needs to provide substantial evidence supporting the assumption that all workers will be provided with gloves impervious to HBCD, that workers will consistently wear such gloves, and that workers will replace their gloves whenever contaminated or compromised. • Under the current exposure assumptions, it is not possible for EPA to conclude that dermal exposure to HBCD presents an unreasonable risk.	Gloves are not fully impervious to solvents that can break through or dissolve the glove over time. However, as a particulate with poor absorption, EPA expects that proper glove use will fully mitigate any dermal exposure from HBCD particulates or dust. Therefore, impervious gloves are expected to eliminate dermal exposure to HBCD. Additionally, EPA only has low-medium confidence in occupational dermal risk estimates, and EPA used conservative assumptions for dermal absorption and therefore risks are likely significantly overestimated (Section 4.3.2.1 and 4.3.2.3).
29	**<u>PUBLIC COMMENTS:</u>** **Assumptions: OSHA** • EPA assumes that three general OSHA standards – the Personal Protective Equipment Standard, the Respiratory Protection Standard, and the Hazard Communication Standard – will ensure that workers have access to and use appropriate PPE. o This assertion misstates the substance of those standards and their role in the TSCA risk evaluation process. o OSHA does not require compliance with SDS recommendations;	OSHA data are collected as part of compliance inspections at various types of facilities. Certain industries are typically targeted based on national and regional emphasis programs. Other inspections may be prompted based on complaints or referrals. As a result, OSHA data may underrepresent PPE usage throughout the affected industry. Additionally, because EPA uses the high-end exposure values to account for uncertainties and variabilities in PPE

	there is no legal mandate for employers to implement the recommended controls.	usage, this is accounted for in its unreasonable risk determinations.
51	• EPA provides no evidence of coordination with OSHA or any other appropriate federal departments/agency in order to achieve maximum enforcement of TSCA while imposing the least burdens of duplicative requirements. o It is difficult to evaluate EPA's analysis of the extent to which potential risks from certain conditions of use are addressed by other statutes and regulations. EPA should clarify this analysis. o EPA should provide greater explanation as to how and why the other applicable statutes and regulations and the agencies and/or program offices responsible for overseeing them adequately address the conditions of use excluded from EPA's risk evaluation.	EPA generally assumes compliance with OSHA requirements for protection of workers, including the implementation of the hierarchy of controls. In support of this assumption, EPA used reasonably available information, including public comments, indicating that some employers, particularly in the industrial setting, are providing appropriate engineering or administrative controls or PPE to their employees consistent with OSHA requirements. EPA does not have reasonably available information to support this assumption for each COU; however, EPA does not believe that the Agency must presume, in the absence of such information, a lack of compliance with existing regulatory programs and practices. Rather, EPA assumes there is compliance with worker protection standards unless case-specific facts indicate otherwise, and therefore existing OSHA regulations for worker protection and hazard communication will result in use of appropriate PPE in a manner that achieves the stated APF or PF. EPA's decisions for unreasonable risk to workers are based on high-end exposure estimates, in order to account for the uncertainties related to whether or not workers are using PPE. EPA believes this is a reasonable and appropriate approach that accounts for reasonably available information and professional judgment related to worker protection practices, and addresses uncertainties regarding availability and use of PPE. While there is no OSHA PEL specific to HBCD, EPA relied on the OSHA PEL for dust, or PNOR (Particulates Not Otherwise Regulates), for modeling purposes. Compliance/non-compliance with statutory requirements outside of TSCA is not a component to
55	• There is no OSHA PEL for HBCD; therefore, there is little to no chance OSHA would cite an employer for failing to provide respiratory protection.	
28, 33, 48	• There is no OSHA or National Institution of Occupational Safety and Health standard for HBCD, but EPA evaluated risks to workers by assuming constant use of respirators and gloves.	
55	• The method for determining the appropriate respirator required by OSHA's standards involves measuring employee exposure to a chemical and comparing it to a respirator's effectiveness in reducing those exposures to a specified level. In the absence of mandatory exposure limits for HBCD, there is no reference point for gauging the effectiveness of any given respirator.	
55	• OSHA does not protect public sector workers or construction workers who are classified as independent contractors. o EPA does not discuss how exposure of this group of workers is affected by the assumption of PPE use.	
63	• OSHA recommends eliminating or controlling all serious hazards; using interim controls while developing longer-term solutions; and selecting controls according to the hierarchy of controls. The hierarchy of controls is clear that PPE is the last line of defense and the least effective means of protecting workers from hazards.	

		consider when conducting risk evaluation under TSCA. Compliance/non-compliance issues are addressed under separate enforcement authorities for each statute. Based on public and SACC comments, EPA has determined that construction workers are not likely to wear respirators. Therefore, the risk determination for *Installation* or *Demolition and Disposal of EPS/XPS Foam Insulation* does not assume respirator use.
29	**PUBLIC COMMENTS:** • The Toxic Substances Control Act (TSCA) requires EPA to evaluate risks "without consideration of costs and other non-risk factors," and to determine whether a chemical presents unreasonable risks to "potentially any exposed and susceptible subpopulations." o Compliance with Occupational Safety and Health Administration (OSHA) standards is insufficient to establish the absence of unreasonable risk under TSCA.	Unreasonable risk determinations incorporate all aspects of risk characterization, including risk estimates, uncertainties, likelihood of PPE usage, and other factors. EPA has updated the unreasonable risk determination format for increased clarity regarding the unreasonable risk determination and the risk considerations for each condition of use.