UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
CHEMICAL SAFETY AND
POLLUTION PREVENTION

December 12, 2019

Memorandum

SUBJECT: Transmittal of Meeting Minutes and Final Report for the TSCA Science Advisory Committee on Chemicals 1-Bromopropane Meeting held September 10-12, 2019

TO: Jeffery Morris, PhD
Director
Office of Pollution, Prevention and Toxics

FROM: Tamue Gibson, MS
Designated Federal Official
TSCA Science Advisory Committee on Chemicals
Office of Science Coordination and Policy

THRU: Steven Knott, MS
Executive Secretary
TSCA Science Advisory Committee on Chemicals
Office of Science Coordination and Policy

Hayley Hughes, DrPH, MPH, CSP
Director
Office of Science Coordination and Policy

Please find attached the meeting minutes and final report of the TSCA Science Advisory Committee on Chemicals (SACC) public meeting held in Arlington, Virginia, on September 10-12, 2019. This report addresses the SACC response to a set of scientific issues being considered by the U.S. Environmental Protection Agency regarding the Peer Review for the Draft Risk Evaluation for 1-Bromopropane (1-BP).

Attachment

cc:
Alexandra Dunn
David Fischer
Jeff Morris
Tala Henry
Mark Hartman
Cathy Fehrenbacher
Stanley Barone
Nhan Nguyen
Yvette Selby-Mohamadu
OPP Docket

TSCA Scientific Advisory Committee on Chemicals

Kenneth Portier, PhD
Henry Anderson, MD
Charles Barton, PhD
Steven Bennett, PhD
Sheri Blystone, PhD
Deborah Cory-Slechta, PhD
Holly Davies, PhD
William Doucette, PhD
Kathleen Gilbert, PhD (Retired)
Mark Johnson, PhD
Alan Kaufman, MS
John Kissel, PhD (Retired)
Ruthann Rudel, MS
Daniel Schlenk, PhD
Sheela Sathyanarayana, MD
Catherine Willett, PhD

TSCA SACC Ad Hoc Peer Reviewers

James D. Blando, PhD
George P. Cobb III, PhD
David A. Eastmond, PhD
Edward J. Perkins, PhD
Isaac N. Pessah, PhD
Michael R. Twiss, PhD
Charles V. Vorhees, PhD

TSCA Science Advisory Committee on Chemicals Meeting Minutes and Final Report No. 2019-03

Peer Review for the United States Environmental Protection Agency (EPA) Draft Risk Evaluation for 1-Bromopropane (1-BP)

September 10-12, 2019

TSCA Science Advisory Committee on Chemicals Meeting

Held at the Hyatt Regency Crystal City at Reagan National Airport 2799 Jefferson Davis Highway Arlington, Virginia

NOTICE

The Toxic Substances Control Act (TSCA) Science Advisory Committee on Chemicals (SACC) is a Federal advisory Committee operating in accordance with the Federal Advisory Committee Act and established under the provisions of TSCA as amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act of 2016. The TSCA SACC provides independent advice and recommendations to the U.S. Environmental Protection Agency (EPA or Agency) on the scientific basis for risk assessments, methodologies, and pollution prevention measures and approaches for chemicals regulated under the Toxic Substances Control Act (TSCA). The SACC serves as a primary scientific peer review mechanism of the EPA, Office of Pollution Prevention and Toxics (OPPT), and is structured to provide balanced expert assessment of chemicals and chemical-related matters facing the Agency. Additional peer reviewers are considered and from time-to-time added on an *ad hoc* basis to assist in reviews conducted by the TSCA SACC. This document constitutes the meeting minutes and final report and is provided as part of the activities of the TSCA SACC.

The TSCA SACC carefully considered all information provided and presented by the Agency, as well as information presented by the public. The minutes represent the views and recommendations of the TSCA SACC and do not necessarily represent the views and policies of the Agency, nor of other agencies in the Executive Branch of the Federal government. Mention of trade names or commercial products does not constitute an endorsement or recommendation for use.

The meeting minutes and final report do not create or confer legal rights or impose any legally binding requirements on the Agency or any party. The meeting minutes and final report of the September 10-12, 2019, TSCA SACC meeting represent the SACC's consideration and review of scientific issues associated with "Peer Review for EPA Draft Risk Evaluation of 1-Bromopropane." Steven Knott, MS, TSCA SACC Executive Secretary, reviewed the minutes and final report. Kenneth Portier, PhD, TSCA SACC Chair, and Tamue Gibson, MS, TSCA SACC Designated Federal Official, certified the minutes and final report. The report is publicly available on the SACC website (https://www.epa.gov/tsca-peer-review) under the heading of "Meetings" and in the public e-docket, Docket No. EPA-HQ-OPPT-2019-0235, accessible through the docket portal: https://www.regulations.gov. Further information about TSCA SACC reports and activities can be obtained from its website at: https://www.epa.gov/tsca-peer-review. Interested persons are invited to contact Tamue Gibson, MS, SACC Designated Federal Official, via e-mail at gibson.tamue@epa.gov.

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TSCA Science Advisory Committee on Chemicals
Meeting Minutes and Final Report
No. 2019-03

Peer Review for EPA Draft Risk Evaluation for 1-Bromopropane (1-BP)

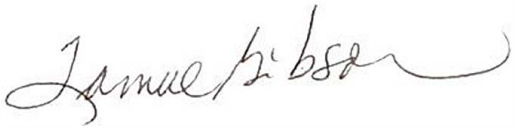
September 10-12, 2019

TSCA Science Advisory Committee on Chemicals Meeting

Held at the Hyatt Regency Crystal City at Reagan National Airport
2799 Jefferson Davis Highway
Arlington, Virginia

Kenneth Portier, PhD
TSCA SACC, Chair
TSCA Science Advisory Committee on Chemicals

Date: 12/11/2019



Tamue Gibson, MS
Designated Federal Official
TSCA Science Advisory Committee on Chemicals

Date: 12/12/2019

Toxic Substance Control Act
Science Advisory Committee on Chemicals Meeting
September 10-12, 2019

Peer Review for EPA Draft Risk Evaluation of
1-Bromopropane (1-BP)

PARTICIPANTS

TSCA SACC, Chair

Kenneth Portier, PhD (Retired), Formerly American Cancer Society, Consulting Biostatistician
Athens, Georgia

Designated Federal Official

Tamue Gibson, MS, TSCA Science Advisory Committee on Chemicals Staff, Office of Science Coordination and Policy, EPA

TSCA Science Advisory Committee on Chemicals Members

Henry Anderson, MD
University of Wisconsin-Madison
Madison, Wisconsin

Charles Barton, PhD
Independent Consultant
Alpharetta, Georgia

Steven Bennett, PhD
Household & Commercial Products Association
Washington, District of Columbia

Sheri Blystone, PhD
SNF Holding Company
Riceboro, Georgia

Deborah Cory-Slechta, PhD
Department of Environmental Medicine
University of Rochester School of Medicine & Dentistry
Rochester, New York

Holly Davies, PhD
Washington State Department of Health
Tumwater, Washington

William Doucette, PhD
Utah State University
Logan, Utah

Kathleen Gilbert, PhD (Retired)
University of Arkansas for Medical Sciences
Little Rock, Arkansas and
Colorado State University
Fort Collins, Colorado

Mark Johnson, PhD
US Army Public Health Center
Aberdeen Proving Ground, Maryland

Alan Kaufman, MS
Toy Industry Association
New York, New York

John Kissel, PhD (Retired)
University of Washington
Seattle, Washington

Ruthann Rudel, MS
Silent Spring Institute
Newton, Massachusetts

Daniel Schlenk, PhD
University of California, Riverside
Riverside, California

Sheela Sathyanarayana, MD
Seattle Research Institute
Seattle, Washington

Catherine Willett, PhD
The Humane Society of the United States
Washington, District of Columbia

TSCA SACC Ad Hoc Peer Reviewers

James D. Blando, PhD
Old Dominion University
Norfolk, Virginia

George P. Cobb III, PhD
Department of Environmental Science
Baylor University
Waco, Texas

David A. Eastmond, PhD
Department of Molecular, Cell and Systems Biology
University of California, Riverside
Riverside, California

Edward J. Perkins, PhD
Environmental Networks and Genetic Toxicology,
U.S. Army Engineer Research & Development Center
Vicksburg, Mississippi

Isaac N. Pessah, PhD
Department of Molecular Biosciences
School of Veterinary Medicine
University of California, Davis
Davis, California

Michael R. Twiss, PhD
Professor of Biology and Director at the Great Rivers Center
Clarkson University
Potsdam, New York

Charles V. Vorhees, PhD
University of Cincinnati College of Medicine and Division of Neurology
Cincinnati Children's Research Foundation
Cincinnati, Ohio

LIST OF ACRONYMS AND ABBREVIATIONS

ACGIH	American Conference of Governmental Industrial Hygienists
AOPs	Adverse Outcomes Pathways
AMAP	Arctic Monitoring and Assessment Programme
BCF	Bioconcentration factors
BMD	Benchmark Dose
BMC	Benchmark Concentration
CEM	Consumer Exposure Model
CI	Confidence Intervals
COU	Conditions of Use
DQE	Data Quality Evaluation
DRE	Draft Risk Evaluation
HEC	Human Equivalent Concentrations
HED	Human Equivalent Dose
HHE	Health Hazard Evaluation
LC50	Lethal Concentration Dose of 50% of the Exposed Population
LEV	Local Exhaust Ventilation
LOAEL	Lowest Observed Adverse Effect Level
MOA	Mode of Action
MOE	Margin of Exposure
MMOA	Mutagenic Mode of Action
NOAEL	No Observed Adverse Effect Level
NIOSH	National Institute for Occupational Safety
OSHA	Occupational Safety and Health Administration
PEL	Permissible Exposure Limit
PESS	Potentially Exposed or Susceptible Subpopulations
POD	Point of Departure
QSAR	Quantitative Structure Activity Relationship
REL	Recommended Exposure Limit
RQ	Risk Quotients
SACC	Science Advisory Committee on Chemicals
SDS	Safety Data Sheet
SR	Systematic Review
TLV	Threshold Limit Value
TSCA	Toxic Substances Control Act
UF	Uncertainty Factor
UF_a	Intra-species Uncertainty Factor
UF_l	LOAEL to NOAEL Uncertainty Factor
VOC	Volatile Organic Compounds
WOE	Weight of Evidence

INTRODUCTION

The Toxic Substances Control Act (TSCA) of 1976, as amended by The Frank R. Lautenberg Chemical Safety for the 21st Century Act in 2016, Science Advisory Committee on Chemicals (SACC) completed its review of the set of scientific issues being considered by the Environmental Protection Agency (EPA) regarding the Draft Risk Evaluation for 1-Bromopropane. The Draft Risk Evaluation, supplemental files, and related documents in support of the SACC peer review meeting are posted in the public e-docket at https://www.regulations.gov (ID: EPA-HQ-OPPT-2019-0235). The initial notice of availability of the Draft Risk Evaluation, opening the docket for comments, and notice of meeting was published in the *Federal Register* on August 12, 2019 (84 FR 39830). The review was conducted in an open Committee meeting held in Arlington, Virginia, on September 10-12, 2019. Dr. Kenneth Portier chaired the meeting. Tamue Gibson, MS, served as the Designated Federal Official.

In preparing these meeting minutes and final report, the Committee carefully considered all information provided and presented by the Agency presenters, as well as information presented by public commenters. These meeting minutes and final report address the information provided and presented at the meeting, especially the Committee response to the Agency charge.

The U.S. EPA presentation was provided during the TSCA SACC meeting by the following (listed in order of presentation):

September 10-12, 2019:

Opening of Meeting – Tamue Gibson, MS, Designated Federal Official, EPA/Office of Science Coordination and Policy (OSCP)

Introduction and Identification of SACC Members – Kenneth Portier, PhD, TSCA Science Advisory Committee on Chemicals (SACC), Chair

Introduction and Welcome – Mark Hartman, EPA/Office of Chemical Safety and Pollution Prevention, Office of Pollution, Prevention and Toxics (OPPT)/ Immediate Office

OPPT Technical Presentation – Overview of 1-Bromopropane Risk Evaluation - Katherine Anitole, Ph.D., EPA/OPPT/RAD

PUBLIC COMMENTERS

Oral statements were presented by:

Stephanie Schwarz, Legal Fellow, Environmental Defense Fund

Lindsay McCormick, Program Manager, Environmental Defense Fund

Richard Denison, PhD, Lead Senior Scientist, Environmental Defense Fund

Robert Sussman, Safer Chemicals Healthy Families

Suzanne Hartigan, PhD, American Chemistry Council

Jonathan Kalmuss-Katz, JD, EarthJustice

Tracey Woodruff, PhD, University of California, San Francisco

Robert Miller, Jr., Senior Director, Global Product Stewardship, Albemarle Corporation

Richard Morford, General Counsel, Enviro Tech International, Inc.

Written statements were provided by:

Written statements were provided as follows:

Jay Tourighy, Senior Vice President, MicroCare Corporation

Michelle Roos, Environmental Protection Network

Suzanne Hartigan, PhD, Senior Director, Regulatory and Technical Affairs, American Chemistry Council

Adam Finkel, ScD, CIH, Clinical Professor of Environmental Health Sciences, University of Michigan School of Public Health

Ben Gann, Director, Chemical Products & Technology Division, American Chemistry Council

Laura Reinhard, Vice President and General Manager, Honeywell

Robert Miller, Jr., Senior Director, Global Product Stewardship, Albemarle Corporation

Jonathan Kalmuss-Katz, JD, Eve C. Gartner and Tosh Sargar, EarthJustice

Enviro Tech International, Inc.

Lindsay McCormick, Chemicals and Health Program Manager, Environmental Defense Fund

Executive Summary

Systematic Review

EPA has continued to improve the application and clarity of the TSCA Systematic Review (SR) as presented in the draft risk evaluation reports reviewed by the Committee so far. However, the SACC continued to recommend and encourage the EPA to proceed with third party review of the SR as soon as possible. The Committee also discussed challenges in following how the studies identified for data integration during the SR were applied throughout the draft evaluation. Members noted that studies identified for data integration were difficult to match with references cited in the bibliography. There are occasional cases where key references and data used in the risk characterization did not go through data quality evaluation (DQE) at all, although that is the Committee's expectation. Members noted that there were multiple instances where the explanation of why papers rated highly in the DQE but not used in the draft risk evaluation was missing or incomplete. The Committee identified at least one instance where a study was rated low under data quality evaluation based on a reference not being available. Committee members were able to readily obtain that reference in the public literature with a simple search. Examples such as this suggest that there is continued room for improvement in EPA's internal processes for SR. The Committee also identified several areas where corrections or additional clarification is needed.

Occupational Exposure Assessment

Overall, the Committee found the occupational exposure assessments to be a useful tool for making decisions about chemical safety. While there is always room for improvement and specific suggestions are listed below, it should be noted that this assessment is suitable and valuable for the task of evaluating the occupational risk associated with 1-BP.

Consumer Exposure Assessment

In general, the Committee agreed that the draft risk evaluation of 1-Bromopropane contained a broad description of consumer exposures and that information presented was well referenced and documented. But the Committee remained unclear as to whether the consumer uses reflected are fully reflective of today's marketplace. The Committee appreciated the inclusion of the 1987 Westat Survey, which remains the most useful survey of consumer exposures, although there are concerns that information is no longer reflective of current consumer use patterns and exposures and, therefore, the Committee recommended inclusion of information from other sources whenever possible. The Committee appreciated the detailed discussion of uncertainty and limitations in the consumer exposure section and encouraged a similar treatment of uncertainty to the extent possible. While inclusion of dermal models was appreciated, the description of dermal model selection was less than adequate and the discussion of dermal exposure with respect to fraction absorbed was unsatisfactory. Therefore, the Committee recommended these sections be expanded. The Committee also appreciated the inclusion of occluded use scenarios but they were concerns that discussion and associated uncertainty of occluded use scenarios was inadequately described.

Environmental Hazard and Risk Characterization

In general, the Committee found Environmental Hazard and Risk Characterization for 1-BP much more refined than for the previously reviewed chemicals. Once again, Committee members also found EPA's PowerPoint summary presented at the TSCA SACC meeting very helpful and several members suggested that the presentation serve as an outline for the executive summary section of this and future risk assessments. The Committee noted that the uncertainties and limitations slides following each hazard and risk characterization section were particularly useful.

The Committee recommended that terms like low, medium or high solubility should be avoided unless they are consistently and appropriately used throughout the document and the measured or estimated value should be listed in parenthesis behind the description. Similarly, terms like highly volatile should also be avoided unless a specific environmental scenario is presented since volatilization depends on the environmental phase (water, soil, sediment, etc.) that the chemical is in and the environmental conditions (temperature, wind speed) associated with the adjacent phase. Several times within the draft risk evaluation, it was stated that the concentration of 1-BP was zero in several environmental compartments based on its high vapor pressure and Henry's constant (e.g., page 180). The Committee noted that it's incorrect to assume zero concentrations in any phase based on equilibrium partition coefficients. No information on kinetics or rates of flux from one phase to another can be implied from equilibrium properties. Committee members also stated several times that sorption to environmental solids was expected to be low. Even with a relatively low Koc value of 40, the concentration of 1-BP in soil or sediment organic matter is 40 times higher than the water and is likely greater than that since sorption to non-organic solid components can also be important in some cases. For example, sorption of relatively volatile solvents to soils is typically higher in dry soils than wet soils because moisture tends to occupy the surface sites associated with clays (e.g., Unger et al., 1996).

Some of the key physical chemical fate properties for 1-BP used in the environmental fate assessments were estimated using EPA's EPISuite program. For some properties, there are several methods that can be used to estimate a value. For example, Koc values can be estimated from experimental Kow values (yielded a value of 66) or from structure derived molecular connectivity indices (MCIs) (yielded a value of 40). Thus, the specific method(s) within EPISuite that was used should be documented. In another case, Henry's constant was estimated using a vapor pressure and aqueous solubility ratio. However, both the Pv and S values that were used came from a secondary reference (a book chapter) instead of the original primary reference (Table 1.1).

One Committee member suggested that when experimental values were available for physical chemical properties, the EPISuite estimates should also be provided to help increase the confidence in the experimental values, especially those obtained from compilations or secondary references.

Finally, several Committee members suggested that in the future, EPA evaluate similar compounds (e.g., halogenated solvents) during the same Committee meeting since they often have similar uses and environmental fate properties.

Human Health Hazard and Dose-Response Assessments

The Committee commended EPA for adding the dermal exposure assessment in response to a previous review of the 2016 draft risk assessment. The inclusion here was very useful. The assumption used seemed reasonable and strength in human equivalent concentrations (HECs) comes from comparing the human exposure with HECs derived from controlled animal data (after uncertainty factors (UFs) are implied). This is qualitatively done, but not as a data integration step in the primary document. The Committee encouraged the EPA to consider providing an evidence integration step within the hazard assessment section integrating controlled animal, human, and relevant mechanistic and *in vitro*, read-across, and in silico information to help support refined HECs inclusive of UFs. In addition, inclusion of an estimate of combined oral and dermal exposure would be welcome.

The Committee found that the use of the nested modeling approach to account for litter effects seemed appropriate under the circumstances. The endpoints used to calculate the POD also seemed appropriate. In general, the Committee was satisfied with this section of the draft risk evaluation.

1-Bromopropane belongs to the haloalkane class of chemicals and can bind to DNA *in vitro* and in vivo. Structurally related haloalkanes are mutagenic and/or carcinogenic. 1-BP has often shown positive results when tested for genotoxicity *in vitro* but has exhibited largely negative results when tested in vivo. Committee members had mixed opinions as to whether the EPA should conclude that 1-BP acts through a mutagenic mode of action. Some Committee members felt that the negative *in vivo* results should be given priority over the *in vitro* assays, and as a result, recommended that the EPA conclude that the MOA for 1-BP is unknown. Others felt that the EPA should be precautionary, and while acknowledging the uncertainty, were of the opinion that the evidence was sufficient to conclude that 1-BP acts through a mutagenic MOA.

The Committee found that the usual multistage models using both 0.1% added risk and 10% extra risk to calculate benchmark concentration (BMC) and the 95% lower confidence limits to calculate benchmark concentration limit (BMCL) (in ppm) seemed appropriate. In addition, to assess the impact of model uncertainty, BMCs (and BMCLs) were also calculated using model averaging approaches. The results calculated by the models were similar (less than one log different). For example, BMCs (benchmark response (BMR) 0.1% AR) for male F344 rats keratoacanthoma/squamous cell carcinoma were 2.96, 3.73 and 9.81 ppm. The BMCL were even closer: 1.78, 2.25, and 1.47 ppm. This kind of consistency using the three models provided support to the accuracy of the BMC calculated for the cancer risk. In general, the Committee thought the averaging approach to obtaining the POD for cancer assessment was appropriate.

In addition to multistage modeling, two model averaging approaches were used in determining the POD for cancer risk. Although there were some concerns about certain parameters, such as physiological interspecies differences between rodents and humans, most of the assumptions of the multistage modeling approach for determining the POD in the cancer assessment were found acceptable by the Committee. In calculating the Inhalation Unit Risk for humans exposed via inhalation based on respiratory carcinomas in mice, the inhalation unit risk (IUR) determined by the multistage modeling (8×10^{-7}) was similar to that determined by the Bayesian modeling (1 x

10^{-6}). This provides support for the multistage modeling approach. There are, however, a number of corrections and additions required to strengthen this section.

Human Health Risk Characterization

In this draft risk evaluation, the WIL Research study (2001) was used to estimate the non-cancer risks to workers and occupational non-users following chronic and acute inhalation exposures to 1-BP. The endpoints of decreased live litter size and increased post-implantation loss (WIL Research, 2001) were used to assess risk from acute exposure to 1-BP. These specific developmental effects were shown in the draft risk evaluation to be the most sensitive endpoint and the one on which was calculated the HEC/dermal human equivalent dose (HED) for an acute exposure duration. This endpoint is also considered to be biologically relevant for the potentially exposed or susceptible subpopulation (e.g., adults of reproductive age and their offspring). The Committee found these endpoints appropriate but recommended that more explanation needs to be added to the draft risk evaluation to justify the use of a chronic exposure scenario in setting the HED for acute effects. Also, more justification is needed to understand why neurotoxicity and immunotoxicity are not used in assessing non-cancer risk.

The Committee had no recommendation and few comments on the question of alternative data that could be used to establish points of departure, or on the selection of uncertainty factor values used in deriving the benchmark MOE for acute inhalation exposures for workers and occupational non-users. The draft risk evaluation used the same approaches for all people-workers, occupational non-users, and consumers.

In general, the Committee had no concerns with the assumptions used to estimate extra lifetime cancer risks to workers which EPA-derived from an inhalation unit risk based on lung tumors in female mice following chronic exposure to 1-BP. The Committee noted that the model averaging was a definite strength of the assessment. As noted above, the only concern was the lack of an estimate of increased cancer risk from short-term exposure to 1-BP.

The draft risk evaluation contains one section with assumptions, key sources of uncertainty, and data limitations for all of the risk assessments. The Committee noted that while some people may find it useful to have all of the assumptions, key uncertainties, and data limitations in one place in the DRE, it is appropriate to discuss each one where they occur throughout the risk evaluation. Similarly, the response to this question overlaps with issues that have been raised in responses to other questions. This response will not be comprehensive and many of the issues raised here are more fully discussed in the Committee's responses to other questions in this report. The Committee recommended the EPA identify key issues that may affect the risk determination, while following the Committee's recommendations on these issues in the responses to other questions in this report; add more references to support assumptions, and quantify assumptions, key uncertainties, and data limitations as much as possible.

The Committee noted that consideration of potentially exposed or susceptible subpopulations (PESS) under TSCA is new and challenging and considers the approach in this draft risk evaluation to be inadequate to address PESS risk. EPA noted the age profiles of the workers included, but that does not by itself adequately characterize the risk. The Committee also

commented that EPA did not consider aggregate exposure risk, since the different exposure estimates were not added together or aggregated.

General Risk Characterization

The Committee commended the Agency staff members who are working directly on completing these complex assessments. The 1-BP assessment has many attributes that represent significant improvements from previous TSCA assessments that have been reviewed by the TSCA SACC members. The Committee appreciated these refinements.

The Committee has confidence that the scientists and engineers assembling and performing these risk assessments selected studies in an objective fashion. The Committee appreciated the Agency's work in the consumer product exposure section in utilizing imperfect data. The Committee appreciated the solid description of uncertainties in Mode of Action for the Human Health Assessment. However, the Committee encountered difficulty in following the exclusion criteria, by which available literature was significantly winnowed to a small percent of available studies. The Committee noted a lack of reproductive and developmental data in the environmental exposure assessment. Without these data, the environmental assessment is quite uncertain. Toxicity determinations were also based on two studies in a single species, with no consideration of whether this was a sensitive species. Given the paucity of toxicity data for the environmental assessment, the Committee recommended inclusion of additional Adjustment Factors or Uncertainty Factors (AFs or UFs) to minimize the likelihood of reaching a false negative conclusion in this determination.

Several statements in the draft risk evaluation state or imply more rigor in procedures and more certainty in hazard determination than some on the Committee felt is justified. This includes aspects of the environmental assessment and the human health assessment. Specific examples are noted in the detailed response to specific charge questions.

The Committee noted uncertainties in defining/identifying occupational non-users, and in excluding potential exposure routes, exposure durations, and magnitude of effect. The Committee pointed out that the assumption that Personal Protective Equipment (PPE) would be used consistently and by all workers is overly optimistic and the draft risk evaluation provided no data to support these assumptions. The Committee expressed concern that the draft risk evaluation does not fully evaluate all sensitive populations, including children and other groups.

The Committee found that the draft risk evaluation failed to consider cumulative or aggregate exposures. It was pointed out that a worker who is occupationally exposed may also be exposed through other conditions of use in the home. Yet, these exposures are decoupled in the draft risk evaluation. The Committee was concerned that 1-BP off-gassing from insulation in home and schools is inadequately assessed, thereby underestimating exposures. It is difficult to determine what fraction of the BPMA biomarker that is found in the general population results from 1-BP. The Committee recommended that this uncertainty should be captured and more thoroughly explained.

The Committee noted a problem in the construct of the P_Der2b model. Additionally, vapor uptake from dermal exposure is not assessed. This omission is a simple example of the failure to assess aggregate exposures.

Overall, the Committee concurred that even though data provided in the DRE underestimated risk, these data did support the finding of unreasonable risk to consumers and occupational conditions, including occupational non-users. Conversely, inadequate data were presented for a robust risk characterization for the environmental assessment, and the information provided did not support the conclusion of "no unreasonable risk to the environment." The lack of consideration for general population exposures excludes a vast extent of the US population (workers, consumers, school children, and other populations) who are exposed to 1-BP, perhaps on a daily basis. The lack of consideration of the general population exposure is concerning given the strong evidence of widespread exposure to a chemical that may be 1-BP based (from biomonitoring data).Many of these problems stemmed from a reduction in the Scope of this assessment during the time since the 2016 Draft Problem Formulation. Many members of the Committee found this reduction in scope troubling.

Content and Organization

The Committee recommended that the organization and presentation made by the EPA in the oral summary be used to structure the written documentation of the draft risk evaluation of 1-BP.

The Committee found several instances where improvements can be made to enhance clarity of the technical and general information provided in the draft risk evaluation. The Committee recommended that an additional summary in lay language be included with the Executive Summary.

The Adverse Outcomes Pathways (AOPs) conceptual modeling approach can be used to understand 1-BP effects and hazards and are capable of ready conveyance of a large set of information to a reader. AOPs provide a causal framework linking molecular initiating events to essential key events and ultimately adverse outcomes of regulatory concern and the Committee recommended this approach. The conceptual model presented in the draft risk evaluation of 1-BP excludes some important reasonably anticipated exposure pathways, especially general population exposure from local indoor and outdoor air concentrations associated with consumer and industrial uses. The document should be explicit that some scenarios presented are out of scope. Finally, the Committee provided details on specific changes to presentation that should be incorporated into the final text to ensure clarity and consistency in expression of concepts and numerical information.

DETAILED COMMITTEE DISCUSSION AND RECOMMENDATIONS – 1-Bromopropane (1-BP)

As amended by the Frank R. Lautenberg Chemical Safety for the 21st Century Act on June 22, 2016, the Toxic Substances Control Act (TSCA), requires the U.S. Environmental Protection Agency (EPA) to conduct risk evaluations on existing chemicals. In response to this requirement, EPA has prepared and published a Draft Risk Evaluation for 1-BP. The risk evaluation for 1-Bromopropane (1-BP) is the fourth to undergo a peer review by the Science Advisory Committee on Chemicals (SACC). The Risk Evaluation process is the second step, following Prioritization and before Risk Management, in EPA's existing chemical process under TSCA. The purpose of risk evaluation is to determine whether a chemical substance presents an unreasonable risk to health or the environment, under the conditions of use, including an unreasonable risk to a relevant potentially exposed or susceptible subpopulation. As part of this process, EPA must evaluate both hazard and exposure, exclude consideration of costs or other non-risk factors, use scientific information and approaches in a manner that is consistent with the requirements in TSCA for the best available science, and ensure decisions are based on the weight-of-scientific-evidence.

The following are the SACC's responses to the Agency's charge questions.

1. ***Systematic Review*** **(Draft Risk Evaluation and Supplemental Files) (Section 1.5 and supplemental documentation)**

   To meet the TSCA scientific standards, EPA applied systematic review approaches and methods to support the draft risk evaluation of 1-BP. Information on the approaches and/or methods is described in the draft risk evaluation as well as the following documents:

   - Application of Systematic Review in TSCA Risk Evaluations (U.S. EPA, 2018a)
   - Strategy for Conducting Literature Searches for 1-BP: Supplemental Document for the TSCA Scope Document (U.S. EPA, 2017b)
   - 1-BP (CASRN: 106-94-5) Bibliography: Supplemental File for the TSCA Scope Document {EPA-HQ-OPPT-2016-0741-0047)}
   - Scope of the Risk Evaluation for 1-BP (U.S. EPA, 2017a)
   - Problem Formulation for 1-Bromopropane (U.S. EPA, 2018b)
   - Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Fate and Transport Studies (EPA, 2019e)
   - Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction Tables for Environmental Fate and Transport Studies (EPA, 2019b)
   - Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data (EPA, 2019f)
   - Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Environmental Release and Occupational Exposure Data for Common Sources (EPA, 2019g)

- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation for Consumer Exposure (EPA, 2019a)
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Extraction for Consumer Exposure (EPA, 2019c)
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Ecological Hazard Studies (EPA, 2019d)
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Updates to the Data Quality Criteria for Epidemiological Studies (EPA, 2019j)
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies – Epidemiologic Studies (EPA, 2019i)
- Draft Risk Evaluation for 1-Bromopropane (1-BP), Systematic Review Supplemental File: Data Quality Evaluation of Human Health Hazard Studies (EPA, 2019h)

Q 1.1	*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 1-Bromopropane (1-BP).*
Q 1.2	*Please also comment on the clarity of the information as presented related to systematic review and suggest improvements as warranted.*

RESPONSE:

The Toxic Substance Control Act (TSCA) Systematic Review (SR) lays the foundation for the draft risk evaluation. While the EPA has continued to improve the application and clarity of the SR as presented in the draft risk evaluation (DRE) reports reviewed by the Committee so far, the Committee again called for the Agency to pursue independent peer review of the SR as soon as possible.

One Committee member evaluated the metric for methodology in the data quality evaluation (DQE) for Environmental Release and Occupational Exposure for 1-BP and in the DQE for Environmental Release and Occupational Exposure Common Sources that may be used for the first ten risk evaluations. The member noted that the criteria for scoring certain sources such as King County in the State of Washington as "high" is not in the SR methodology (Application of Systematic Review in TSCA Risk Evaluations, U.S. EPA, 2018a), nor is being published in a scientific or peer-reviewed journal, which was a commonly noted as a viable reason for scoring "high" on methodology. Some Members observed that evaluators scored the sources as "high" if it was derived from the Agency or from another federal agency. Other state and local agencies mentioned are Toxics Use Reduction Institute (TURI), California Air Resources Board (CARB), and a consultant funded by CARB. Studies from academic labs, manufacturers, the European Chemicals Agency (ECHA), Halogenated Solvents Industry Alliance, Inc. (HSIA) were also rated high. Authors that were not rated high for methodology included Northeast Waste Management Officials' Association (NEWMOA), National Toxicology Program (NTP), Agency for Toxic Substance and Disease Registry (ATSDR), Occupational Safety and Health Administration (OSHA), Japanese Ministry of the Environment. The Committee member noted

this as an example of inconsistency in following the Agency's published methodology for systematic review.

The Committee noted that the criteria for occupational exposure (U.S. EPA, 2018a) specifies that the only way to obtain an unacceptable score for methodology is when the methodology is explained, and the EPA is aware that it is unacceptable. If an explanation is omitted, the score is determined to be low. The EPA explains "The reason for this approach is to avoid omitting potentially valid data or information since occupational exposure and release data are often sparse." This is very different from the approach on human health hazard, which has much more stringent criteria for scoring and if any element is evaluated as unacceptable, the paper is rated unacceptable. The Committee recommended that the criteria for different types of information should be more consistent.

In regard to "Sample size", the Committee noted this designation's definition (U.S. EPA 2018a) is not an actual sample size, but whether there are statistical derivations to describe the sample size. They also noted that there is no established process to obtain an unacceptable score. Some Committee members recommended this element be renamed to reflect the definition.

"Metadata" is one criterion for sample types, exposure types, sample durations, exposure durations, worker activities, and exposure frequency. This criterion is not comparable to the human health hazard evaluation where all of the data were evaluated more stringently and separately. Again, there is no established process to obtain an unacceptable score for metadata.

For Example: on page 98 of the DRE, a question was posed by the Committee as to why the Agency did not use four specific papers in the risk evaluation, but the Hanley references were determined to be "High" in the DQE. If the four studies were determined to be inferior for the risk evaluation, then they should not have been determined to be of "High" quality. Alternatively, if these four studies were deemed of high quality, they should have been included in the risk evaluation. The explanation of why sources rated "high" were not used needs improvement. This is another example of the difficulty the Committee experienced reconciling information between the SR and the DRE.

Another Committee member noted there were many models used that were not reviewed in the DQE, though there are established criteria in the 2018 document on Application of Systematic Review. The EPISuite model was evaluated under fate and transport, though there are no criteria for evaluating models under fate. Further, modeling data is noted as a source of fate data. When EPISuite was evaluated most metrics were designated as "N/A". For environmental release and occupational exposure, there is a section describing how to evaluate models, however, none of the models were evaluated. Perhaps because this is for published models and the models they selected were not published.

One Committee member discussed how the EPA identified consumer uses as not being described in the SR and the sources were not reviewed through the DQE. There are 10 sources in the DQE for the consumer exposure assessment with little or no explanation as to why most are not used in the DRE. Another Committee member questioned whether the statement "All three parameters had a range of documented values within literature identified as part of Systematic Review" located on page 115 of the DRE is accurate.

Another Committee member discussed how the SR process was used only for dose-response and was not used for the entire DRE for the Human Health Hazard (Figures 1-10, page 48 of the DRE). The DRE states "the influential information sources used to support quantitative analyses represents a smaller pool of studies that were ultimately subjected to the TSCA systematic review process to ensure that the risk evaluation uses the best available science in the overall weight of evidence." The Committee noted that it would be helpful to define those terms. The Committee member noted that key and supporting studies were not subject to data quality evaluation through the systematic review process. "Only the key and supporting studies carried forward for dose-response analysis in the 2016 Draft Risk Assessment for 1-BP (U.S. EPA, 2016d), and any new studies published since that time, were subjected to the TSCA systematic review process." The DRE also mentioned "informal evaluation for overall data quality and relevance." This informal process was not explained.

All of the studies used for the dose-response in the DRE were evaluated in the DQE.
As noted in the excel spreadsheets (located in the public docket at https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0057 under the "On topic sub-spreadsheet" with docket ID number: 2019-0235-0057), one study was rated unacceptable because the study duration of male fertility was completed in 6 weeks instead of the OECD study protocol minimum of 8 weeks. Nonetheless, this study was cited several times (five) in the DRE without mention of an unacceptable score. One Committee member commented that this occurrence is an example of overly stringent criteria for human health hazard studies, especially when compared to occupational studies. Based on the length of the male reproductive cycle in mice, six weeks is an adequate timeframe, even if eight weeks is the standard assay length. In addition, there was another human health study with an unacceptable criterion that was not rated unacceptable overall, even though the methodology requires that (U.S. EPA 2018a).

Committee members also noted in section 3.2.3 for Toxicokinetics, page 145 of the DRE, that there were no SR criteria and that all information were derived from "previous regulatory and non-regulatory chemical assessments", which may have been "informally evaluated for overall data quality and relevance." These terms were not defined and were not clear if the sources from the foundational reviews were evaluated (or not) for data quality. The same references were used in the previous section 3.2.8 on Evidence Integration and Evaluation of Human Health Hazards page 159 of the DRE. A Committee member described the appearance of a typical literature search and summary versus a systematic review with data integration.

Several Committee members discussed in depth that it was not appropriate to determine an "unacceptable" rating during data quality evaluation based solely on one criterion.

Another Committee member stated that section 3.2.4 on Biomarkers of Exposure page 148 of the DRE consisted of an adequate summary of biomonitoring, but it was not listed in the literature search or other parts of the systematic review.

One Committee member noted they reviewed the regulatory requirements for systematic review and determined systematic review is not included in TSCA the law. The EPA has interpreted the new scientific standards in the revised TSCA law to include systematic review and the Agency wrote it into the definition of weight of evidence in rulemaking. The same Committee member

noted the absence in the rulemaking language regarding the use of systematic review for dose-response and that TSCA does not limit scientific standards to dose response.

Committee members reviewed the DRE to understand how the systematic review was used. The Committee expected all of the quality sources identified in the SR would be used in the DRE and if not, that the general public would be able to follow the rationale as to why they were not used. The Committee generally concluded that it was difficult at best to determine exactly what was done during the SR. The assessment presented an outline of what was done, and referenced documents provided more information, however it did not specify what decision criteria were used to exclude specific items from the evaluation. Committee members expressed that they experienced challenges in trying to follow the actions taken in the SR, and how the results of the SR were used in the draft risk assessment. Specific recommendations are provided at the end of this discussion.

One Committee member noted that the literature review for fate and transport data consisted of only atmospheric routes and should also have included groundwater and sediment routes of exposure. The Committee member felt this error likely stems from a faulty conceptual model or problem formulation. Thus, there is no assessment of 1-BP in groundwater even though the Agency states on page 51 that 1-BP "is expected to exhibit low adsorption to soils and thus can migrate rapidly through soil to groundwater." Further, it was also noted, that atmospheric routes are the sole mention of an exposure route in the DRE in its entirety. Many jurisdictions do not regulate groundwater quality when used by individual property owners as drinking water. The same Committee member noted that the assessment should include this aspect OR state clearly that individuals consuming groundwater are likely to experience higher exposures than estimated by this assessment.

Some Committee members reviewed and commented on how all of the on topic sources in the bibliography were evaluated for data quality and used in the DRE, starting with the Environmental Fate and Transport Data Sources (Figures 1-6 of the DRE, page 44). The Committee discussed that the information in the bibliography and data quality evaluation did not match the information in Figures 1-6. For example, there are nine "on topic" peer reviewed references from the bibliography, none of which are included in the data quality evaluation (DQE) for Environmental Fate and Transport (Table 2-1). There are seven studies in Table 2-1 whereas Figures 1-6 lists 18 studies as being evaluated. Four of the seven studies referenced in Table 2-1 were derived from existing Office of Pollution Prevention and Toxics (OPPT) sources. The sources of the remaining three studies are unclear. One of the on topic bibliographic sources that was not in the DQE is included in the DRE references. According to Figures 1-6, twelve studies were excluded during data evaluation, however, none were rated as unacceptable based on the evaluation criteria. The Committee also noted that the sources on environmental fate and transport were mostly cited in the DRE in Table 2-1, 2.1.1 and Appendix C. Table 2-1 has two other references that were not evaluated in the DQE. One of them is referred to as "High" and the other is referred to as "Low" even though neither were evaluated for data quality. Several Committee members noted that the one reference rated "Low" in Table 2-1 received this rating because a source reference was not available. Committee members were easily able to find this reference with a simple search.

A Committee member identified similar issues for other data categories in Figures 1-6 through 1-9 of the DRE pages 44-55. The results of the evaluation are available in the power point presentation slides located in the public docket https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0058 under the "Supporting Documents" section with docket ID number: 2019-0235-0058. The excel spreadsheet documents are available in the public docket https://www.regulations.gov/document?D=EPA-HQ-OPPT-2019-0235-0057 under the "Supporting Documents" section with docket ID number: 2019-0235-0057.

The Committee member concluded the following:

- Fewer than 25% of the references cited in the DRE were evaluated for data quality.
- All of the studies used for dose-response were evaluated for data quality.
- The methodology for data quality evaluation is flawed and was not always followed by the evaluators.
- The methodology for data quality evaluation is uneven across different types of sources
- The high percentage (>95%) of excluded references suggests the original search could be improved.
- It is not clear how sources were identified and why specific sources were or were not used in the DRE.

Description of Systematic Review Excel Spreadsheets

Each DQE supplementary document has its own Excel spreadsheet.

Systematic Review3.xlsx

Excel file with Multiple Spreadsheets

1. On topic spreadsheet- all of the on topic sources with which search they were done for and whether they appear in the DQE (and if so, what the score is). It's not complete, but for some it was noted when they were not evaluated in the DQE and were found in the references.
2. RE references spreadsheet- All of the references from the draft risk evaluation. The EPA references that were not in the literature search or the DQE are not included. The analysis is not complete, but for some it is noted how the reference was identified (where it was derived from) and the results if it was in the DQE.
3. DQE EFT spreadsheet- Sources in the Data Quality Evaluation for Environmental Fate and Transport with scores, notes, how the reference was identified (where it was derived from), how they were used in the DRE, and what other papers were used for the fate and transport table 2-1 of the DRE.
4. DQE EROE spreadsheet- Sources in the Data Quality Evaluation for Environmental Release and Occupational Exposure with category, score, notes, Methodology score and why the evaluator gave it that methodology score from the DQE.
5. DQE EROECS spreadsheet- Sources in the Data Quality Evaluation for Environmental Release and Occupational Exposure: Common Sources used in the first ten risk

evaluations. With category, score, notes, Methodology score and why the evaluator gave it that methodology score from the DQE.

6. DQE CE spreadsheet- Sources in the Data Quality Evaluation for Consumer Exposure with category, score, notes, how the reference was identified (where it was derived from), and whether the data was extracted.
7. DQE EH spreadsheet- Source in the Data Quality Evaluation for Ecological Hazard with its score and notes.
8. DQE HHEE spreadsheet- Sources in the Data Quality Evaluation for Human Health Hazard Epidemiologic with scores and how the reference was identified (where it was derived from)
9. DQE HHH spreadsheet- Sources in the Data Quality Evaluation for Human Health Hazard with category, score, and notes.
10. Ref and DQE spreadsheet- Comparison showing which references in DRE were evaluated in DQE.

Description of Each PowerPoint Slides (by Slide Number)

Systematic review PPP.pptx

1. DRE Figures 1-6 Literature Flow Diagram for Environmental Fate and Transport Data Sources. The notes describe the differences between this figure and what the Committee member found in the bibliography and data quality evaluation supplemental files.
2. Fate. This figure complements the Excel spreadsheets, especially DQE EFT. How the sources were used in the DRE is also noted, but not in the figure. The figure describes
   - How the on topic sources for fate in the bibliography were or were not evaluated for data quality
   - Where the references in the Data Quality Evaluation for Environmental Fate and Transport came from and their relationship to the literature search bibliography.
3. Figures 1-7. Literature Flow Diagram for Environmental Release and Occupational Exposure Data Sources. The notes describe the differences between this figure and what the Committee member found in the bibliography and data quality evaluation supplemental files.
4. Engineering. This figure complements the Excel spreadsheets, especially DQE EROE. The figure describes:
   - How the on topic sources for engineering in the bibliography were or were not evaluated for data quality
   - Where the references in the Data Quality Evaluation for Engineering Releases and Occupational Exposure came from and their relationship to the literature search bibliography.
5. Figures 1-8. Literature Flow Diagram for Consumer and Environmental Exposure Data Sources. The notes describe the differences between this figure and what the Committee member found in the bibliography and data quality evaluation supplemental files.

6. Exposure and Consumer Exposure. This figure complements the Excel spreadsheets, especially DQE CE. The figure describes
    - How the on topic sources for Exposure in the bibliography were or were not evaluated for data quality
    - Where the references in the Data Quality Evaluation for Consumer Exposure came from and their relationship to the literature search bibliography.
7. Figures 1-9. Literature Flow Diagram for Environmental Hazard Data Sources. The notes describe the differences between this figure and what the Committee member found in the bibliography and data quality evaluation supplemental files.
8. Environmental Hazard and Ecological Hazard.
9. Figures 1-10. Literature Flow Diagram for Human Health Hazard Data Sources. The notes describe the differences between this figure and what the Committee member found in the bibliography and data quality evaluation supplemental files.
10. Human Health Hazard
11. The apparent role of the SR in this DRE. There were many pathways for references to be included in the DRE and most references were not reviewed for data quality in the DQE. Fewer than 25% of the 282 references in the DRE have DQE scores.
12. Expected role of systematic review in this DRE.

Recommendations to Improve the TSCA Systematic Review:

- Define terms and use them consistently.
- Ensure all sources of information used in the DRE undergo the systematic review and be explicit where they are derived from.
- Use a consistent citation style throughout the systematic review to make it easier to follow specific references.
- Improve clarity and explanation when data identified during the literature search from one topic is relevant and used for a different topic. Consider improvements to the search terms to ensure relevant data is found.
- The names for the criteria should match what they are. For example, “sample size” for occupational studies should be renamed to reflect it is about statistical description.
- Standardize criteria across categories of data as much as possible.
- Studies should be retained even if they are not appropriate for dose-response. For example, animal models with only one concentration may still have useful information.
- Improve the use of “grey literature” and peer review literature. As in past DREs, this DRE has government studies in the “peer reviewed literature.”
- Improve the clarity of data integration. Multiple times papers that had been identified for data extraction and integration were not used with no explanation as to why.
- Under the heading for Executive Summary, 8th bulleted item for conditions of use, page 20, appears to contradict the exclusion criteria presented earlier in the Executive Summary. Cleaning and degreasing products were excluded according to the executive summary (page 19) and should be clarified.
- Since large percentages of studies are excluded (Section 1.5.1, page 42), the number of items being rejected for each criterion should be summarized to enable readers to determine why studies were excluded.

- Consider whether the exclusion of large percentages of studies suggests that the search strategy could be improved.
- Update the SR criteria for Methodology/Reliability for Environmental Release and Exposure to reflect current practices or adapt procedures to ensure current criteria are applied consistently.
- Consider defining or further describing data that are "only considered potentially relevant data/information sources and were used qualitatively" within the SR.
- 1-BP_SR Supplemental File for Data Quality Evaluation of Environmental Fate and Transport Studies indicates the rationale for downgrading the quality rating for a key reference on hydrolysis half-life, namely "Mabey, W; Mill, T. (1978). Critical review of hydrolysis of organic compounds in water under environmental conditions [Review]. J Phys Chem Ref Data 7: 383-415. HERO ID: 9848" was quoted as "Article not useful without cited reference". The missing reference (Laughton, 1959) is readily available and located on page 85 within the Reference section of this document.
- Consider the following Recommendations from the 2017 1-BP Literature Strategy document:

    - Correct page 5 and page 8 of the strategy document where the text "ERROR! Reference not found" appears.
    - Include atmosph* in the search terms for exposure, engineering, & fate on page 22 of the strategy document (Table_Apx B-1).
    - Verify that Appendix C2 page 30 entry 1013 - Office of Air: Ambient Water Quality Criteria Docs – is accurate. Is this entry associated with the Office of Water?
    - Page 69, Table E1 indicates that Environmental persistence data were included if they were: "Studies that indicate persistence, transformation, AND degradation in the environment." Should this be OR? Similar comment for Bioaccumulation
    - Page 80. It is unclear if the 4th inclusion criterion: "The paper is a publicly available document", means that the document can be downloaded without a subscription or if this means published in journal, book, or other outlet that can be accessed with or without cost. This should be clarified.

2. *Occupational Exposure Assessment* (Section 2.3.1 of the Draft Risk Evaluation)

EPA evaluated acute and chronic exposures to workers for conditions of use in industrial and commercial settings. For exposure via the inhalation pathway, EPA quantified occupational exposures for both workers and occupational non-users based on a combination of monitoring data and modeled exposure concentrations. For exposure via the dermal route, EPA modeled exposure for workers, accounting for the effect of volatilization and glove use. EPA assumed dermal exposure would not occur for occupational non-users.

EPA assumed that workers and occupational non-users would be adults of both sexes (>16 and older, including women of reproductive age) based on occupational work permits.

Q 2.1	*Please comment on the approaches and estimation methods, models, and data used in the occupational exposure assessment.*